(23)

No. 04-607

DEC 23 2005

IN THE

Supreme Court of the United States

LABORATORY CORPORATION OF AMERICA HOLDINGS (doing business as LabCorp),

Petitioner,

v.

METABOLITE LABORATORIES, INC. and COMPETITIVE TECHNOLOGIES, INC.,

Respondents.

On Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

JOINT APPENDIX
(Volume I of II)

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PETITION FOR CERTIORARI FILED NOVEMBER 3, 2004
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SUPPLEMENTAL APPENDIX

United States Patent No. 4,940,658 (July 10, 1990)

The appendix to the petition for certiorari contains the following material which is omitted from the Joint Appendix:

Appendix A:

Opinion of the U.S. Court of Appeals for the Federal Circuit dated June 8, 2004 ..... 1a

Appendix B:

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Appendix C:

Order of the U.S. Court of Appeals for the Federal Circuit Denying Rehearing and Rehearing En Banc dated August 5, 2004 ..... 40a

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

No. 03-1120

METABOLITE LABORATORIES, INC.
and COMPETITIVE TECHNOLOGIES, INC.,
Plaintiffs-Appellees,

v.

LABORATORY CORPORATION OF AMERICA
HOLDINGS (doing business as LabCorp),
Defendant-Appellant.

DOCKET ENTRIES

DATE	FILINGS – PROCEEDINGS
2/19/03	CORRECTED BRIEF for Appellant Laboratory Corporation of America Holdings. By Laboratory Corporation (Appellant). Served by mail on 3/12/2003. Filed on 2/19/2003. (Non-confidential)
4/21/03	BRIEF for Appellees. By Metabolite Laboratories, Inc. & Competitive Technologies, Inc. (Appellees). Served by mail on 4/21/2003. Filed on 4/21/2003. (Non-confidential)
5/8/03	REPLY BRIEF for Appellant Laboratory Corporation of America Holdings (d/b/a LabCorp). By Laboratory Corporation of America (d/b/a LabCorp) (Appellant). Served by mail on 5/8/2003. Filed on 5/8/2003. (Non-confidential)

5/15/03	JOINT APPENDIX (5 volumes). By Laboratory Corporation of America Holdings (Appellant). Served by mail on 5/15/2003. Filed on 5/15/2003. (Non-confidential)
6/30/03	SUPPLEMENTAL APPENDIX. By Metabolite Technologies, Inc. (Appellant). Served by mail on 6/9/2003. Filed on 6/30/2003. (Non-confidential)
11/5/03	ORAL ARGUMENT DATE / Calendared
6/8/04	DISPOSITION: AFFIRMED; by PANEL
8/12/04	MANDATED

U.S. DISTRICT COURT
DISTRICT OF COLORADO (DENVER)

CIVIL DOCKET FOR CASE #: 1:99-cv-00870-ZLW-CBS

METABOLITE LABORATORIES, INC.,
a Colorado corporation, and

COMPETITIVE TECHNOLOGIES, INC.,
a Delaware corporation,

Plaintiffs,

v.

LABORATORY CORPORATION OF AMERICA HOLDINGS (d/b/a LABCORP),
a Delaware corporation,

Defendant.

DOCKET ENTRIES

DATE	NO.	PROCEEDINGS
05/04/1999	1	COMPLAINT (Summons(es) issued); jury demand (former empl) (Entered: 05/05/1999)
07/19/1999	3	AMENDED COMPLAINT [1-1] by plaintiff; jury demand (former empl) (Entered: 07/20/1999)
07/20/1999	5	RETURN OF SERVICE of Summons and Complaint upon / by defendant Laboratory Corp Amer on 7/19/99 (former empl) (Entered: 07/22/1999)

08/30/1999	11	ANSWER to complaint [3-1] and COUNTERCLAIM; jury demand by defendant Laboratory Corp Amer against plaintiff (former empl) (Entered: 09/01/1999)
09/15/1999	12	REPLY TO COUNTERCLAIM [11-2] by counter-defendant Metabolite Labs Inc, counter-defendant Competitive Tech Inc (former empl) (Entered: 09/16/1999)
01/31/2000	31	Unopposed MOTION by plaintiff to file second amended cmp (former empl) (Entered: 02/01/2000)
01/31/2000		Tendered Second Amd Cmp submitted by plaintiff re: motion to file second amended cmp [31-1] (former empl) (Entered: 02/01/2000)
01/31/2000	32	MOTION by defendant Laboratory Corp Amer to file under seal mtn for leave to amend answer/cntclms (former empl) (Entered: 02/01/2000)
01/31/2000	33	MOTION by defendant Laboratory Corp Amer for leave to amend answer and cntclms (filed under seal) (former empl) (Entered: 02/01/2000)
02/02/2000	34	MINUTE ORDER : by Judge Zita L. Weinshienk granting motion to file second amended cmp [31-1] and clerk to file stamp tendered second amd cmp (cc: all counsel) ; entry date : 2/3/00 (former empl) (Entered: 02/03/2000)
02/02/2000	35	Second AMENDED COMPLAINT by plaintiff; jury demand; adding defendant Peter Wentz (former empl) (Entered: 02/03/2000)

02/14/2000	41	REPLY TO amended COUNTER-CLAIM [11-2] by counter-defendant (former empl) (Entered: 02/15/2000)
02/29/2000	49	AMENDED ANSWER [11-1] by defendant Laboratory Corp Amer; jury demand (gms) (Entered: 10/17/2001)
02/29/2000	49	AMENDED COUNTERCLAIM [11-2] by counter-claimant Laboratory Corp Amer (gms) (Entered: 10/17/2001)
03/03/2000	50	Third AMENDED COMPLAINT by plaintiff; jury demand (former empl) (Entered: 03/06/2000)
03/15/2000	52	ANSWER by defendant Laboratory Corp Amer to third amended complaint [50-1]; jury demand (gms) (Entered: 10/17/2001)
03/15/2000	52	AMENDED COUNTERCLAIM [11-2] to 3rd amd cmp by counterclaimant Laboratory Corp Amer (gms) (Entered: 10/17/2001)
03/28/2000	53	REPLY TO Amended COUNTER-CLAIMS [52-1] by counter-defendants Metabolite & Competitive (gms) (Entered: 10/17/2001)
07/31/2000	91	COURTROOM MINUTES by Judge Zita L. Weinshienk GRANTING motion to dismiss for lack of jurisdiction converted to motion for summary jgm [69-1]; dismissing party Peter Wentz on condition that he will be available as witness for trial; entry date: 8/9/00 Court Reporter: Kara Spitler (former empl) (Entered: 08/09/2000)

08/07/2000	87	MOTION by defendant Laboratory Corp Amer for summary judgment (gms) (Entered: 08/07/2000)
08/07/2000	88	Memorandum (BRIEF) by defendant Laboratory Corp Amer in support of motion for summary judgment [87-1] (gms) (Entered: 08/07/2000)
08/07/2000	89	APPENDIX filed by defendant Laboratory Corp Amer to motion for summary judgment [87-1] (gms) (Entered: 08/07/2000)
08/07/2000	90	MOTION by plaintiffs for summary judgment on patent infringement claim against deft Lab Corp of Amer Hldgs (former empl) (Entered: 08/08/2000)
08/07/2000	92	ORDER OF DISMISSAL by Judge Zita L. Weinshienk: GRANTING motion to dismiss for lack of jurisdiction converted to motion for summary jgm [69-1]; DISMISSING party Peter Wentz on condition that he will be available as witness on trial (cc: all counsel) entry date: 8/9/00 (former empl) (Entered: 08/09/2000)
08/14/2000	93	MINUTE ORDER : by Judge Zita L. Weinshienk setting hearing on each party's motion for summary judgment on patent infringement claim against deft Lab Corp of Amer Hldgs [90-1] & motion for summary judgment [87-1] 9:00 10/4/00. Responses to opposing party's motion is due 8/27/00, replies due 9/11/00. (cc: all counsel) ; entry date : 8/14/00 (gms) (Entered: 08/14/2000)
08/25/2000	94	Amended MINUTE ORDER : by Judge Zita L. Weinshienk regarding [93-1]

		minute order. Each party to file resp in opp to motion for sum jgm by 8/28/00 and each party may reply by 9/12/00. Setting hearing on motion for summary judgment on patent infringement claim against deft Lab Corp of Amer Hldgs [90-1] 9:00 10/4/00, setting hearing on motion for summary judgment [87-1] 9:00 10/4/00 (cc: all counsel) ; entry date: 8/25/00 (gms) (Entered: 08/25/2000)
08/28/2000	95	Memorandum (BRIEF) by defendant Laboratory Corp Amer in opposition to motion for summary judgment [90-1] (lam) (Entered: 08/28/2000)
08/28/2000	96	APPENDIX filed by defendant Laboratory Corp Amer to opposition brief [95-1] to motion for summary judgment [90-1] (lam) (Entered: 08/28/2000)
08/28/2000	97	RESPONSE by plaintiffs to motion for summary judgment [87-1] (former empl) (Entered: 08/29/2000)
09/12/2000	99	REPLY by defendant Laboratory Corp Amer to response to motion for summary judgment [87-1] (former empl) (Entered: 09/14/2000)
09/12/2000	100	APPENDIX filed by defendant Laboratory Corp Amer to motion reply [99-1] (former empl) (Entered: 09/14/2000)
09/12/2000	101	APPENDIX BI-BK filed by defendant Laboratory Corp Amer to motion reply (filed under seal) [99-1] (former empl) (Entered: 09/14/2000)
09/12/2000	102	MOTION by defendant Laboratory Corp Amer to seal appendix BI-BK to reply to

Motion for Summary Jgm. (former empl) (Entered: 09/14/2000)

09/12/2000 103 REPLY by plaintiff to response to motion for summary judgment on patent infringement claim against deft Lab Corp of Amer Hldgs [90-1] (former empl) (Entered: 09/14/2000)

10/04/2000 105 COURTROOM MINUTES by Judge Zita L. Weinshienk denying motion for summary judgment on patent infringement claim against deft Lab Corp of Amer Hldgs [90-1], denying motion for summary judgment [87-1] ; entry date : 10/6/00 Court Reporter: Paul Zuckerman (former empl) (Entered: 10/06/2000)

10/06/2000 106 ORDER by Judge Zita L. Weinshienk denying pla's motion for summaryjudgment on patent infringement claim against deft Lab Corp of Amer Hldgs [90-1], denying dft's motion for summary judgment [87-1] (cc: all counsel) ; entry date : 10/10/00 (former empl) (Entered: 10/10/2000)

11/02/2000 112 MarkmanBRIEF FILED by defendant Laboratory Corp Amer (former empl) (Entered: 11/03/2000)

11/02/2000 113 Claim Construction BRIEF FILED by defendant Laboratory Corp Amer (oversized document, placed on oversized document shelf) (former empl) Modified on 11/03/2000 (Entered: 11/03/2000)

11/09/2000 114 Claim Construction Response BRIEF FILED by plaintiffs (former empl) (Entered: 11/13/2000)

11/09/2000	115	RESPONSE by defendant Laboratory Corp Amer to plfs' claim construction brief [114-1] (former empl) (Entered: 11/13/2000)
11/16/2000	116	COURTROOM MINUTES by Judge Zita L. Weinshienk ; in court hrg/Markman Hearing held 11/16/00. Court will issue an order and state the scope of claim 13. Simultaneous cross motions for sum jgm due 1/5/01, reply briefs to these motions due 1/17/01 ; entry date : 11/21/00 Court Reporter: Paul Zuckerman (gms) (Entered: 11/21/2000)
11/21/2000	117	TRANSCRIPT of Markman Hearing on November 16, 2000 before Judge Zita L. Weinshienk (pages: 1-66) Prepared By: Paul Zuckerman (certified copy) (former empl) (Entered: 11/22/2000)
11/29/2000	118	ORDER by Judge Zita L. Weinshienk regarding [116-2] minutes. Term "detecting" in claim 13 is construed to mean "determining the existence of", "deficiency" to mean "a shortage of a substance necessary to health","elevated" to mean "raised above the normal range" and "correlating" to mean "to establish a mutual or reciprocal relationship between" (cc: all counsel) ; entry date : 11/30/00 (gms) (Entered: 11/30/2000)
01/05/2001	120	Renewed MOTION by defendant Laboratory Corp Amer for summary judgment (former empl) (Entered: 01/08/2001)
01/05/2001	121	MOTION by plaintiff Metabolite Labs Inc, plaintiff Competitive Tech Inc for

partial summary judgment (former empl) (Entered: 01/08/2001)

01/05/2001 122 APPENDIX in Support filed by defendant Laboratory Corp Amer to their renewed motion for summary judgment [120-1] (former empl) (Entered: 01/08/2001)

01/17/2001 127 RESPONSE (titled reply) by defendant Laboratory Corp Amer to pla's motion for partial summary judgment [121-1] (former empl) (Entered: 01/17/2001)

01/17/2001 128 APPENDIX S to dft's response to pla's motion for partial sum jgm, filed by defendant Laboratory Corp Amer under seal [127-1], re: motion to file under seal [126-1] (former empl) (Entered: 01/17/2001)

01/17/2001 129 RESPONSE by plaintiffs to dft's renewed motion for summary judgment [120-1] (former empl) (Entered: 01/18/2001)

01/23/2001 133 REPLY by plaintiff to dft's response to pla's motion for partial summary judgment [121-1] (titled: pla's surreply to dft's reply to pla's motion for partial sum jgm and motion to file same) (former empl) (Entered: 01/24/2001)

01/23/2001 133 MOTION by plaintiffs for leave to file surreply to dft's response to pla's motion for partial sum jgm with surreply incorporated in motion (former empl) (Entered: 01/24/2001)

02/12/2001 136 Opposition (RESPONSE) by counterclaimant Laboratory Corp Amer to motion for leave to file surreply to dft's re-

		sponse to pla's motion for partial sum jgm [133-1] (lam) (Entered: 02/14/2001)
02/22/2001	140	MOTION by Pla Metabolite Labs Inc, and Pla Competitive Tech Inc to strike from the final pre-trial order Labcorp's unpled defenses and claims and undisclosed witness (erv) (Entered: 02/27/2001)
02/22/2001	141	OBJECTIONS by Dft Laboratory Corp America and to motion to strike certain claims/defenses as set forth by Pla's in the final pre-trial order undisclosed witness [140-1] (erv) (Entered: 02/27/2001)
02/26/2001	143	FINAL PRE-TRIAL ORDER to Magistrate Judge Craig B. Shaffer (cc: all counsel) (erv) (Entered: 02/28/2001)
03/01/2001	170	COURTROOM MINUTES by Judge Zita L. Weinshienk ORDERED: 1) As to Pla's Motion for Partial Summary Judgment seeking a declaration that Claim 13 covers LabCorp's performance of the Panel Test, Ruling is reserved until the validity of Claim 13 is decided by fact-finder. ORDERED 2) DENYING motion for partial summary judgment seeking a declaration that Claim 13 covers LabCorp's performance of the Homocysteine-only test. [121-1], ORDERED 3) GRANTING Dft's motion for summary judgment seeking a declaration that Claim 13 and 33 do not cover LabCorp's performance of the Homocysteine-only test [120-1] ORDERED: 4) Dft's Motion for Summary Judgment seeking a Declaration that claim 13 and 33 are invalid is DENIED. ORDERED: 5) Pla's Motion for Partial Summary Judgment seeking a

		Declaration that Claim 18 covers LabCorp's performance of the Panel test is GRANTED. ORDERED: 6) Dfts' Motion for Summary Judgment seeking a Declaration that LabCorp does not induce infringement of Claim 13 and Claim 33 is DENIED. ORDERED: 7) Dfts' Motion for Summary Judgment on the issue of validity of Claim 13 and Claim 33 is DENIED.; entry date : 3/21/01 Court Reporter: Paul Zuckerman (erv) (Entered: 03/21/2001)
03/02/2001	144	RESPONSE by Dft Laboratory Corp Amer ("Lab Corp") to Pla's motion to strike from the final pre-trial order Labcorp's unpled defenses and claims and undisclosed witness [140-1] (erv) (Entered: 03/05/2001)
03/02/2001	145	REPLY by Pla Metabolite Labs Inc to Dfts' Objection and motion to strike from the final pre-trial order Labcorp's unpled defenses claims and undisclosed witness [140-1] (erv) (Entered: 03/05/2001)
03/06/2001	146	TRANSCRIPT of hrg on motions for Summary Judgment on 3-1-01 before Judge Zita Weinsheink, (pages: 1-23) Prepared By: Paul Zuckerman (certified copy) (erv) (Entered: 03/08/2001)
03/07/2001	147	TRANSCRIPT of Excerpts from hrg on Dft's motion to dismiss on 7/31/00 before Judge Zita Weinshienk (pages: 1-5) Prepared By: Kara Spitler (certified copy) (erv) (Entered: 03/08/2001)
03/08/2001	148	MOTION by Pla Metabolite Labs Inc,and Pla Competitive Tech Inc in

limine to restrict or exclude Dft's Expert Testimony (erv) (Entered: 03/12/2001)

03/08/2001 149 MOTION by Pla Metabolite Labs Inc, and Pla Competitive Tech Inc in limine to prevent Labcorp from introducing evidence or taking positions at trial that contradict previous admissions made by Labcorp (erv) (Entered: 03/12/2001)

03/08/2001 150 MOTION by Pla Metabolite Labs Inc, and Pla Competitive Tech Inc in limine to allow Jury view of Metabolite's assay procedures and know how (erv) (Entered: 03/12/2001)

03/08/2001 151 MOTION by Pla Metabolite Labs Inc, and Pla Competitive Tech Inc in limine to Require Labcorp to make Certain of its Employee Witnesses Available during Plas' case-in Chief (erv) (Entered: 03/12/2001)

03/08/2001 152 MOTION by Dft Laboratory Corp Amer in limine to Prevent Plas' from offering Parol Evidence re: the Patent License Agreement (erv) (Entered: 03/12/2001)

03/08/2001 153 MOTION by Dft Laboratory Corp Amer in limine to prevent Plas from referring to any alleged consequences of any mistakes in Labcorp's material (erv) (Entered: 03/12/2001)

03/08/2001 154 MOTION by Dft Laboratory Corp Amer in limine to prevent Plas from arguing or referring during Trial that Labcorp infringes or willfully infringes the 658 Patent (erv) (Entered: 03/12/2001)

03/08/2001 155 MOTION by Dft Laboratory Corp Amer in limine to Exclude Plas from making

		reference in any manner regarding Abbott indemnification and licensing issues (erv) (Entered: 03/12/2001)
03/08/2001	156	MOTION by DFT Laboratory Corp Amer in limine to exclude references to Royalty Payment issues previously resolved. (erv) (Entered: 03/12/2001)
03/08/2001	157	MOTION by Dft Laboratory Corp Amer in limine to exclude Plas from referring to any evidence regarding settlement of unrelated items (erv) (Entered: 03/12/2001)
03/13/2001	158	OBJECTIONS by defendant Laboratory Corp Amer to Pla's Trial Exhibits (erv) (Entered: 03/14/2001)
03/13/2001	159	OBJECTIONS by Plas' Metabolite Labs Inc, and Competitive Tech Inc to s' Designated exhibits. (Rule 26(a)(3) (erv) (Entered: 03/15/2001)
03/15/2001	160	RESPONSE by plaintiffs to dft's motion in limine to Exclude Plas from making reference in any manner regarding Abbott indemnification and licensing issues [155-1] (former empl) (Entered: 03/19/2001)
03/15/2001	161	RESPONSE by plaintiffs to dft Labcorp's motion in limine to prevent Plas from referring to any alleged consequences of any mistakes in Labcorp's material [153-1] (former empl) (Entered: 03/19/2001)
03/15/2001	162	RESPONSE by plaintiffs to dft's motion in limine to prevent Plas from arguing or referring during Trial that Labcorp infringes or willfully infringes the 658 Pat-

ent [154-1] (former empl) (Entered: 03/19/2001)

03/15/2001 163 RESPONSE by plaintiffs to dft's motion in limine to exclude references to Royalty Payment issues previously resolved. [156-1] (former empl) (Entered: 03/19/2001)

03/15/2001 164 RESPONSE by plaintiffs to dft's motion in limine to exclude Plas from referring to any evidence regarding settlement of unrelated items [157-1] (former empl) (Entered: 03/19/2001)

03/15/2001 165 RESPONSE by defendant Laboratory Corp Amer to pla's motion in limine to allow Jury view of Metabolite's assay procedures and know-how [150-1] (former empl) (Entered: 03/19/2001)

03/15/2001 166 RESPONSE by defendant Laboratory Corp Amer to pla's motion in limine to restrict or exclude Dft's Expert Testimony [148-1] (former empl) (Entered: 03/19/2001)

03/15/2001 167 RESPONSE by defendant to pla's motion in limine to Require Labcorp to make Certain of its Employee Witnesses Available during Plas' case-in Chief [151-1] (former empl) (Entered: 03/19/2001)

03/15/2001 168 RESPONSE by defendant to pla's motion in limine to prevent Labcorp from introducing evidence or taking positions at trial that contradict previous admissions made by Labcorp [149-1] (former empl) (Entered: 03/19/2001)

03/15/2001	169	RESPONSE by plaintiff to dft's motion in limine to Prevent Plas' from offering Parol Evidence re: the Patent License Agreement [152-1] (former empl) (Entered: 03/19/2001)
03/16/2001	171	ORDER by Judge Zita L. Weinshienk re: [121-1] Pla's Motion for Partial Sum Jgm, re: [120-1] Dfts' Motion for Sum Jgm. The matter was be[fo]re the Ct for Oral Argument. The Ct having heard the Arguments and Statements of Csl & made oral conclusions of law which are incorporated by reference as fully set forth. Accordingly, It is ORDERED: that as to Pla's Motn for Partial Sum Jgm seeking a declaration that Claim 13 covers LabCorp's performance of the Panel Test, ruling is reserved until the Validity of Claim 13 is decided by the fact-finder. It is Further Ordered that Pla's Motion for Partial Sum Jgm seeking a declaration that Claim 13 covers LabCorp's performance of the Homocysteine-only test is DENIED., It is Further Ordered that Dfts' motn for Sum Jgm seeking a declaration that Claim 13 and 33 do not cover LabCorp's performance of the Homocysteine-only test is GRANTED. It is Further Ordered that Dfts' Motn for Sum Jgm that Claim 13 and Claim 33 are invalid is DENIED. It is Further Ordered that Pla's mton for Partial Sum Jgm seeking a declaration that Claim 13 covers LabCorp's performance of the Panel Test is GRANTED. It is Further Ordered that Dft's motion for Sum Jgm seeking a declaration that LabCorp does not induce infringement of Claim 13 and Claim 33

		is DENIED. It is Further Ordered that Dfts' Motion for Partial Sum Jgm on issue of validity of Claims 13 and 33 is DENIED. (cc: all counsel) ; entry date : 3/21/01 (erv) (Entered: 03/21/2001)
03/19/2001	172	PRE-TRIAL STATUS REPORT by defendant Laboratory Corp Amer (erv) (Entered: 03/21/2001)
03/19/2001	173	STATUS REPORT by Pla Metabolite Labs Inc, Pla Competitive Tech Inc (erv) (Entered: 03/21/2001)
03/22/2001	179	COURTROOM MINUTES by Judge Zita L. Weinshienk DENYING motion in limine to Require Labcorp to make Certain of its Employee Witnesses Available during Plas' case-in Chief. It is the Cts understanding that Peter Wentz and Denise Hodge will be available. As to the other witnesses Pla wants, the attys shall confer and resolve any remaining disputes. The question of who bears the cost of travel will be decided at the end of trial. The Ct will allow LabCorp to question Mr. Wentz during Pla's case so that he will not be requires to return for Dfts case in chief. [151-1], finding the motion in limine to restrict or Dft's Expert Testimony [148-1] moot as the motion relates to Dr. Wentz, DENYING motion in limine to allow Jury view of Metabolite's assay procedures and know-how [150-1], DENYING motion to strike from the final pre-trial order Labcorp's unpled defenses and claims and undisclosed witness as follows: a) Motion to strike the unpled license defense is DENIED, b) motion to strike the

unpled statutory defense under 35 U.S.C.271(c) is DENIED, c) Motion to strike the copyright subject matter defense is DENIED, d) Motion to strike dfts declarations in their prayer for relief is DENIED as moot, in view of Dfts agreement to amend paragraph five. e) Motion to strike undisclosed witness, Dr. Kang is DENIED, f) Pla may depose Dr. Kang between now and the trial date. The parties shall meet with the Magistrate Judge after the hrg to discuss the need for additional discovery.[140-1], DENYING Pla's motion in limine to prevent Labcorp from introducing evidence or taking positions at trial that contradict previous admissions made by Labcorp [149-1], GRANTING in part and DENYING in part as follows: a) motion to strike reference to unpaid royalties for the panel of tests on pg 15 of the final pretrial order is DENIED b) Motion to strike the issue of whether claims 13 and 18 cover the panel test is DENIED. c) Motion to strike Pla's alleged claim of defense on page 16 of the final pre-trial order is DENIED. d) Motion to strike any reference in footnote 1, page 3 in the claims section of the pre-trial order is DENIED as moot, as the Ct will not consider this a stipulation. e) Dfts request to reserve its right to object to some stmts in the pretrial order they believe are not admissable at trial is GRANTED. [141-1], DENYING motion in limine to Exclude Plas from making reference in any manner regarding Abbott indemnification and licensing issues, with leave to

object at trial if appropriate [155-1], DENYING motion in limine to exclude references to Royalty Payment issues previously resolved. [156-1], DENYING motion in limine to prevent Plas from referring to any alleged consequences of any mistakes in Labcorp's material [153-1], GRANTING motion in limine to exclude Plas from referring to any evidence regarding settlement of unrelated items [157-1], [154-1] The ct reserves ruling on this motion in limine to prevent Plas from arguing or referring during Trial that Labcorp infringes or willfully infringes the 658 Patent,the parties may file a short brief on this issue. regarding [152-1] The Ct reserves ruling on this motion in limine to Prevent Plas' from offering Parol Evidence re: the Patent License Agreement, the parties may file short brief on this issue.; entry date : 4/16/01 Court Reporter: Paul Zuckerman (erv) (Entered: 04/16/2001)

03/26/2001 174 TRANSCRIPT of Trial Preparation Conference and Hrg on Motions on 3/22/01 before Judge Zita Weinshienk (pages: 1-53) Prepared By: Paul Zuckerman (certified copy) (erv) (Entered: 03/27/2001)

04/12/2001 180 ORDER by Judge Zita L. Weinshienk This matter was before the ct on 3/22/01, for oral argument on various motions in limine,objections and motions to strike. The ct heard the arguments and stmts of csl, and made oral conclusions of law which are incorporated herein by reference as if fully set forth, Accordingly, It is ORDERED that Plas' Motion in

limine to require Labcorp to make certain Of its Employee Witnesses availability during Pla's case-in-chief, file 3-8-01, is DENIED. It is the cts understanding that Peter Wentz and Denise Hodge will be available. As to the other requested witnesses, the parties shall confer and resolve any remaining disputes. It is Further ORDERED that Plas' motion in limine to restrict or exclude Dfts Expert testimony, filed 3-8-01 is DENIED. Both Steven Bent and Dr. McCully will be allowed to testify within their area of expertise only. As the motion relates to Dr. Wentz, the motion is Moot. It is Further ORDERED that Pla's motion in limine to allow Jury View of Metabolite's Assay Procedures and Know-How, filed 3-8-01, is DENIED. It is Further ORDERED that Plas' motion to strike from the final pretrial Order Labcorps Unpled Defenses and Claims and Undisclosed Witness, filed 2-22-01 is DENIED as follows: Motion to strike the license defense is DENIED;Motion to strike the statutory defense under 35 U.S.C. 271(c) is DENIED;motion to strike the copyright subject matter defense is DENIED; motion to strike Dfts declaration in their prayer for relief is DENIED as MOOT, in view of the Dfts agreement to amend paragraph five;motion to strike undisclosed witness Dr. Kang, is DENIED. Pla may depose Dr. Kang between now and the trial date. The parties shall meet with the Magistrate JUdge about the necessity for any further discovery. It is Further OR-

DERED that the Plas motion in limine to prevent Labcorp from introducing evidence or taking positions at trial that contradict previous admissions made by Labcorp,filed 3-8-01 is DENIED. It si Further ORDERED that Labcorps obj and motion to strike certian claims/defenses set forth by Plas in the final pretrial order, filed 2/22/01 is DENIED as follows: Motin to strike the issue of whether claims 13 and 18 cover the panel test is DENIED. Motion to strike reference to unpaid royalties for the panel tests on pg 16 of the final pretrial order is DENIED; motion to strike any reference in footnote 1,pg 3 in the claims section of the pretrial order is MOOT, as the ct will not consider it a stipulation.Dfts request to reserve its right to obj to some stmts in the pretrial order it believes are not admissable at trial is GRANTED. It is Further ORDERED that Dfts motion in limine to Exclude Plas from making reference in any mmanner regarding Abbott indemnifiication and Licensing issues, filed 3-8-01 is DENIED with lv to obj at trial if appropriate. It is Further ORDERED that Dfts motion in limine to prevent Plas from referring to any alleged consequences of any mistakes in Labcorps materials, filed 3-8-01 is DENIED with lv to obj at trial is appropriate. It is Further ORDERED that Dfts motion in limine to exclude Plas from referring to any evidence regarding settlement of unrelated matters filed 3-8-01 is GRANTED, subject to chg after consideration of the par-

		ties briefs on the subject. It is Further ORDERED that the ct reserves ruling as to Dft Labcorps motion in limine to prevent Plas from arguing or referring during trial that Labcorp infringes or willfully infringes the 658 patent, filed 3-8-01. It is Further ORDERED that the ct reserves ruling as to Dfts Labcorps motion in limine to prevent Plas from offering Parol Evidence regarding the patent license agreement filed 3-8-01. It is Further ORDERED that the parties may file short briefs on the following issues:1) Admissability of evidence regarding Labcorps settlement with theb govt; 2)whether the existence of metabolites license precludes argument on patent infringement, how the parol evidence rule applies to the specific facts of the case. Briefs shall not exceed 5 pgs and shall be filed on or before 5-18-01 (cc: all counsel) ; entry date : 4/17/01 (erv) (Entered: 04/17/2001)
05/17/2001		Tendered Fourth Amended Complaint submitted by plaintiff Metabolite Labs Inc, plaintiff Competitive Tech Inc re: motion to amend complaint and Jury demand [1-1] in view of results of ct ordered audit and rule 7.1 cert. [181-1] (erv) (Entered: 05/21/2001)
05/17/2001	182	Further BRIEF by Plaf in opposition to motion in limine to prevent Plas from arguing or referring during Trial that Labcorp infringes or willfully infringes the 658 Patent [154-1] (erv) (Entered: 05/21/2001)

05/18/2001	181	MOTION by Pla Metabolite Laboratories, Inc. and Competitive Tech Inc to amend complaint [1-1] in view of results of ct ordered audit and rule 7.1 cert. (erv) (Entered: 05/21/2001)
05/18/2001	183	BRIEF by defendant Laboratory Corp Amer in support of motion in limine to Prevent Plas' from offering Parol Evidence re: the Patent License Agreement [152-1] (erv) (Entered: 05/22/2001)
05/18/2001	184	BRIEF by defendant Laboratory Corp Amer in support of motion in limine to prevent Plas from arguing or referring during Trial that Labcorp infringes or willfully infringes the 658 Patent [154-1] (erv) (Entered: 05/22/2001)
05/18/2001	185	BRIEF by defendant Laboratory Corp Amer in support of motion in limine to exclude Plas from referring to any evidence regarding settlement of unrelated item: [157-1] (erv) (Entered: 05/22/2001)
05/18/2001	186	SUPPLEMENT by defendant Laboratory Corp Amer to brief re: Parol evidence rule [183-1], to motion in limine to Prevent Plas' from offering Parol Evidence re: the Patent License Agreement [152-1] (erv) (Entered: 05/22/2001)
05/18/2001	187	SUPPLEMENT (Further Brief) by Pla Opposing Labcorp's motion to exclude evidence of $187 Million Fraud settlement (erv) (Entered: 05/23/2001)
05/25/2001	193	MINUTE ORDER : by Judge Zita L. Weinshienk regarding Pla's [181-1] motion to amend complaint [1-1] in view of results of ct ordered audit and rule 7.1

cert.,Dft shall file a response brief not to exceed 10 pgs on or before 6/8/01 (cc: all counsel) ; entry date : 5/30/01 (erv) (Entered: 05/30/2001)

05/30/2001 194 RESPONSE by Plas'to brief in support of motion in liomine regarding Parol evidence [183-1] (erv) (Entered: 06/01/2001)

06/08/2001 195 RESPONSE by defendant Laboratory Corp Amer to plas' motion to amend complaint [1-1] in view of results of ct ordered audit and rule 7.1 cert. [181-1] (pap) (Entered: 06/11/2001)

06/11/2001 196 ORDER by Judge Zita L. Weinshienk granting Pla's motion for leave to amend complaint [1-1]; Dft may file appropriate motions in response. Accordingly, it is Ordered that Pla's motion is Granted over objection. in view of results of ct ordered and rule 7.1 cert. [181-1] (cc: all counsel) ; entry date 6/12/01 (erv) (Entered: 06/12/2001)

06/11/2001 197 Fourth AMENDED COMPLAINT by plaintiff Metabolite Labs Inc; jury demand (erv) (Entered: 06/12/2001)

07/02/2001 200 Response (MOTION) by defendant Laboratory Corp Amer to dismiss Pla's 4th Amd Cmp (which is being treated as a mtn for sum jgm per 7/20/01 mo) (dlb) Modified on 07/25/2001 (Entered: 07/03/2001)

07/20/2001 201 MINUTE ORDER : by Judge Zita L. Weinshienk. Labcorp's motion under Rule 12, in response to 4th amd cmp will be treated as a motion for summary judgment. Response brief due 8/8/01, re-

ply brief due 8/22/01, setting hearing on the motion for sum jgm (to dismiss Pla's 4th Amd Cmp) [200-1] 9:30 8/29/01 (cc: all counsel) ; entry date : 7/25/01 (gms) Modified on 09/12/2001 (Entered: 07/25/2001)

08/08/2001 203 RESPONSE by plaintiff Metabolite Labs Inc, plaintiff Competitive Tech Inc to motion to dismiss Pla's 4th Amd Cmp (which is being treated as a mtn for sum jgm per 7/20/01 mo) [200-1] (erv) (Entered: 08/09/2001)

08/22/2001 204 REPLY by Dft Laboratory Corp Amer to Pla's response to motion to dismiss Pla's 4th Amd Cmp (which is being treated as a mtn for sum jgm per 7/20/01 mo) [200-1] (erv) (Entered: 08/23/2001)

09/26/2001 208 ORDER by Judge Zita L. Weinshienk denying Pla's Fourth Amended complaint [197-1], denying Dfts' Lab Corp's motion in limine to Prevent Plas' from offering Parol Evidence re: the Patent License Agreement [152-1], denying Dfts' Lab Corp's motion in limine to prevent Pla's from arguing or referring during Trial that Lab Corp infringes or willfully infringes the '658 patent [201-1] ; Trial prep conference vacated on 9/26/01 An answer shall be filed within 15 days of the 9/17/01 trial prep conf (cc: all counsel) ; entry date : 9/27/01 (erv) (Entered: 09/27/2001)

09/27/2001 209 COURTROOM MINUTES by Judge Zita L. Weinshienk denying Lab Corp's motion to dismiss Pla's 4th Amd Cmp (which is being treated as a mtn for sum jgm per 7/20/01 mo) [200-1],and deny-

ing Lab Corp's in limine to prevent Plas from arguing or referring during Trial that Labcorp infringes or willfully infringes the 658 Patent [154-1] An Answer shall be filed within 15 days of the 9/17/01 trial prep conf. Dfts', by Stipulation,shall have an Officer certify and ratify all reports submitted to Pla's pursuant to section3.02 of the License Agreement, and shall deliver to Pla's within 20 days of the 9/17/01 trial prep conf. ; entry date : 9/28/01 Court Reporter: Paul Zuckerman (erv) (Entered: 09/28/2001)

10/02/2001 211 Second Pretrial STATUS REPORT by defendant Laboratory Corp Amer (erv) (Entered: 10/03/2001)

10/02/2001 210 ANSWER by defendant Laboratory Corp Amer to 4th amended complaint [197-1]; jury demand (gms) (Entered: 10/17/2001)

10/02/2001 210 AMENDED COUNTERCLAIM [11-2] to 4th amended cmp by counter-claimant Laboratory Corp Amer (gms) (Entered: 10/17/2001)

10/02/2001 212 AMENDED ANSWER [11-1] by defendant Laboratory Corp Amer to 4th amended complaint; jury demand (gms) (Entered: 10/17/2001)

10/02/2001 212 AMENDED COUNTERCLAIM [11-2] to 4th amd cmp by counter-claimant Laboratory Corp Amer (gms) (Entered: 10/17/2001)

10/16/2001 213 REPLY TO COUNTERCLAIMS to 4th Amended Cmp [212-1] by counter-defendant Metabolite Labs Inc, counter-

defendant Competitive Tech Inc (gms) (Entered: 10/17/2001)

11/01/2001 214 TRANSCRIPT of Hrg on Motion for Sum Jgm on 10/4/01 before Honorable Zita L. Weinsheink, Judge (pages: 1-18) Prepared By: Paul Zuckerman (certified copy) (erv) (Entered: 11/02/2001)

11/05/2001 222 COURTROOM MINUTES, Jury Trial, Day 1 by Judge Zita L. Weinshienk ; jury trial held 11/5/01 , finding the motion to compel Labcorp to deliver its witheld damages information [217-1] moot ; entry date : 11/8/01 Court Reporter: Paul Zuckerman (gms) (Entered: 11/08/2001)

11/05/2001 224 EXHIBIT list by defendant Laboratory Corp Amer (erv) (Entered: 11/09/2001)

11/05/2001 225 EXHIBIT list by plaintiff Metabolite Labs Inc, plaintiff Competitive Tech Inc (erv) (Entered: 11/09/2001)

11/05/2001 226 Witness list submitted by plaintiff Metabolite Labs Inc, plaintiff Competitive Tech Inc (erv) (Entered: 11/09/2001)

11/06/2001 219 Deposition Designation (STATEMENT) by plaintiff Metabolite Labs Inc, plaintiff Competitive Tech Inc (Excerpts from Depositions) (erv) (Entered: 11/07/2001)

11/06/2001 220 BRIEF FILED by plaintiff Metabolite Labs Inc regarding the acceptance of Dr. Stabler and Dr. Allen as Experts (erv) (Entered: 11/08/2001)

11/06/2001 223 COURTROOM MINUTES, Jury Trial, Day 2 by Judge Zita L. Weinshienk ; entry date : 11/8/01 Court Reporter: Paul Zuckerman (gms) (Entered: 11/08/2001)

11/07/2001	229	COURTROOM MINUTES (Trial to Jury Day-3) by Judge Zita L. Weinshienk ; entry date : 11/9/01 Court Reporter: Paul Zuckerman (erv) (Entered: 11/09/2001)
11/08/2001	230	COURTROOM MINUTES (Trial to Jury Day 4) by Judge Zita L. Weinshienk ; entry date : 11/9/01 Court Reporter: Paul Zuckerman (erv) (Entered: 11/09/2001)
11/09/2001	232	COURTROOM MINUTES (Trial to Jury Day-5) by Judge Zita L. Weinshienk ; entry date : 11/13/01 Court Reporter: Paul Zuckerman] (erv) (Entered: 11/13/2001)
11/13/2001	231	DEPOSITION of Boger Team (Excerpts from Depositions) (erv) (Entered: 11/13/2001)
11/13/2001	234	COURTROOM MINUTES (Trial to Jury Day-6) by Judge Zita L. Weinshienk ; entry date : 11/15/01 Court Reporter: Paul Zuckerman (erv) (Entered: 11/15/2001)
11/14/2001	233	OBJECTIONS by defendant Laboratory Corp Amer and Counterdesignations to Pla's deposition Designations [231-1] (erv) (Entered: 11/14/2001)
11/14/2001	235	Proposed STATEMENT by defendant Laboratory Corp Amer of Uncontested Facts Relating to Notice (erv) (Entered: 11/16/2001)
11/14/2001	236	Proposed STATEMENT by Plas' of Uncontested Facts Relating to Notice (erv) (Entered: 11/16/2001)

11/14/2001	238	COURTROOM MINUTES (Trial to Jury Day 7) by Judge Zita L. Weinshienk ; entry date : 11/16/01 Court Reporter: Paul Zuckerman (erv) (Entered: 11/16/2001)
11/15/2001	240	COURTROOM MINUTES Trial to Jury Day-8 by Judge Zita L. Weinshienk (attached are video/reading depos re: Lai-Goldman, Andress & Novack) ; entry date : 11/20/01 Court Reporter: Paul Zuckerman (erv) Modified on 11/23/2001 (Entered: 11/20/2001)
11/16/2001	239	COURTROOM MINUTES Trial to Jury day-9 by Judge Zita L. Weinshienk. Dfts rule 50 Motion is Denied, Pla's rule 50 Motion is Denied, The Ct reserves the right to reconsider the arguments after the jury returns with a verdict ; entry date : 11/20/01 Court Reporter: Paul Zuckerman (erv) (Entered: 11/20/2001)
11/19/2001	243	COURTROOM MINUTES Trial to Jury Day 10 by Judge Zita L. Weinshienk, Jury Instructions read to the Jury ; entry date : 11/21/01 Court Reporter: Paul Zuckerman (erv) (Entered: 11/21/2001)
11/19/2001	244	Supplemental Memorandum (BRIEF) FILED by defendant Laboratory Corp Amer in support of motion for judgment as a matter of law re: minutes [239-1] (lam) (Entered: 11/23/2001)
11/20/2001	241	COURTROOM MINUTES Trial to Jury Day 11 by Judge Zita L. Weinshienk The Verdict is read into the record. It is ORDERED that the Court will not enter Jgm until 12/3/01. It is Further ORDERED that Dfts to file motions by 12/12/01; At-

tached: Stipulation and Order regarding Custody of Exhibits; Jury Instructions; Jury List; Dfts Exhibit List; Plas Exhibit List; Dfts witness list; Pla's witness list entry date : 11/21/01 Court Reporter: Paul Zuckerman (erv) (Entered: 11/21/2001)

11/20/2001 242 Special VERDICT for plaintiff against defendant; entry date : 11/21/01,The Jury finds that Dft LabCorp is not licensed under the 658 patent and that license has been terminated in whole or in part; That LabCorp has breached its license agreement by terminating it with respect to its performance of the Abbott test; Damages to the Pla Metabolite for the breach of contract in the amt of $3,652,724.61; Dft LabCorp has contributed to and induced infringement of claim 13 of the 658 patent; Damages to Pla CTI caused by the Dft LabCorp's infringement by inducment or by contributory infringement in the amt of $1,019,365.01; LabCorp has willfully infringed calim 13 of the 658 patent; claims 13 and 18 of the 658 patent are not invalid. (erv) (Entered: 11/21/2001)

11/29/2001 245 MOTIONS by defendant Laboratory Corp Amer regarding Verdict,Judgment and Rile 7.1 Compliance (erv) (Entered: 11/30/2001)

12/03/2001 246 JUDGMENT: by Honorable Zita L. Weinsheink, United States District Court Judge pursuant to [242-1] special verdict which is incorporated herein by reference as if fully set forth. Accordingly it is ORDERED that a Jgm is entered in

favor of the Plas' Metabolite Laboratories Inc., and Competitive Technologies and against Dft Laboratory Corporation of America Holdngs. It is Further ORDERED that the damages to be awarded to Pla Metabolite for Dft Lab Corp'"s bearch of contract are $3.652,724.61. It is Further ORDERED that the damages to be awarded to Pla Competitive Technologies, due Dft LabCorp's infringement by inducement or by contributory infringement are $1,019,365.01. It is Further ORDERED that post jgm interest shall accrue at the legal rate of 2.23% per annum from the date of entry of the jgm. dismissing case (cc: all counsel) ; entry date : 12/3/01 (erv) (Entered; 12/03/2001)

12/03/2001	247	Proposed Judgment and Decree (STATEMENT) by plaintiff, as requested by the Ct, and Pla's Stipulation to LabCorp's Proposed Briefing schedule re: judgment [246-2] (erv) (Entered: 12/06/2001)
12/10/2001	248	MOTION by defendant Laboratory Corp Amer to stay execution pending disposition of post trial motions (erv) (Entered: 12/10/2001)
12/12/2001	249	Renewed MOTION by defendant Laboratory Corp Amer for judgment as a matter of law (pap) (Entered: 12/13/2001)
12/12/2001	250	Memorandum (BRIEF) by defendant Laboratory Corp Amer in support of motion for judgment as a matter of law [249-1] (pap) (Entered: 12/13/2001)

12/12/2001	251	MOTION by defendant Laboratory Corp Amer for new trial (pap) (Entered: 12/13/2001)
12/12/2001	252	Memorandum (BRIEF) by defendant Laboratory Corp Amer in support of dft's alternative motion for new trial [251-1] (pap) (Entered: 12/13/2001)
12/12/2001	253	MOTION by defendant Laboratory Corp Amer to alter or amend judgment [246-2] (pap) (Entered: 12/13/2001)
12/12/2001		Proposed FINDINGS of fact and conclusions of law on patent misuse by defendant Laboratory Corp Amer (pap) (Entered: 12/13/2001)
12/12/2001	254	MOTION by plaintiff for enhanced damages , and for attorney fees for willful infringement (pap) (Entered: 12/13/2001)
12/12/2001	255	MOTION by plaintiff for permanent injunction to permanently enjoin dft from performing any homosysteine-only tests (pap) (Entered:12/13/2001)
12/12/2001	256	MOTION by plaintiff Metabolite Labs Inc for order to confirm prejudgment interest (pap) (Entered: 12/13/2001)
12/12/2001	257	MOTION by plaintiff Competitive Tech Inc for order for prejudgment interest (pap) (Entered: 12/13/2001)
12/12/2001	258	Stipulation and Opposition (RESPONSE) by plaintiff to dft's motion to stay execution pending disposition of post trial motions [248-1] (pap) (Entered: 12/13/2001)

12/19/2001	260	REPLY in Support by defendant Laboratory Corp Amer to pla's response to dft's motion to stay execution pending disposition of post trial motions [248-1] (dlb) (Entered: 12/19/2001)
01/09/2002	262	RESPONSE by Plas' Metabolite Labs Inc, Competitive Tech Inc to findings of fact and conclusions of Law on Patent Misuse [0-0], motion to alter or amend judgment [246-2] [253-1] (erv) (Entered: 01/10/2002)
01/09/2002	264	RESPONSE by defendant Laboratory Corp Amer to Plas' motion for enhanced damages [254-1] and Atty fees for willful infringement (erv) (Entered: 01/10/2002)
01/09/2002	266	RESPONSE(Opposition) by defendant Laboratory Corp Amer to Plas' motion for permanent injunction to permanently enjoin dft from performing any homosysteine-only tests [255-1] (erv) (Entered: 01/10/2002)
01/09/2002	263	RESPONSE by plaintiffs to dft's renewed motion for judgment as a matter of law [249-1], and alternative motion for new trial [251-1] (pap) (Entered: 02/28/2002)
01/09/2002	265	RESPONSE by defendant Laboratory Corp Amer to pla's motion for order for prejudgment interest [257-1], pla's motion for order to confirm prejudgment interest [256-1] (pap) (Entered: 02/28/2002)
01/11/2002	267	SUPPLEMENTAL response by defendant Laboratory Corp Amer to Plas' motions for Pre-Jgm interest containing

Treasury Bill Rate calculations [265-1] (pap) (Entered: 02/28/2002)

01/23/2002 269 REPLY by defendant Laboratory Corp Amer to Pla's response to Dfts motion to alter or amend judgment [246-2] [253-1] (erv) (Entered: 01/23/2002)

01/23/2002 272 REPLY Brief by plaintiff Metabolite Labs Inc to motion for permanent injunction to permanently enjoin dft from performing any homosysteine only tests [255-1] (erv) (Entered: 01/24/2002)

01/23/2002 273 REPLY by plaintiff Metabolite Labs Inc to Dfts response to Pla's motion for enhanced damages [254-1] and Atty Fees for Labcorp's willful infringement (erv) (Entered: 01/24/2002)

01/23/2002 268 REPLY in support by defendant Laboratory Corp Amer of its renewed motion for judgment as a matter of law [249-1], motion for new trial [251-1] (pap) (Entered: 02/28/2002)

01/23/2002 271 REPLY by plaintiff Competitive Tech Inc concerning motion for order for prejudgment interest [257-1] (pap) (Entered: 02/28/2002)

01/24/2002 270 REPLY by plaintiff Metabolite Labs Inc to dft's response to Pla's motion for order to confirm prejudgment interest [256-1] (pap) (Entered: 02/28/2002)

02/11/2002 274 MOTION by defendant Laboratory Corp Amer for leave to file corrected Memorandum in Support of Laboratory Corporation of America Holding's Renewed Motion for Jgm as a matter of Law (erv) (Entered: 02/11/2002)

02/11/2002		Tendered Corrected Memorandum submitted by defendant Laboratory Corp Amer re: motion for leave to file corrected Memorandum in Support of Laboratory Corporation of America Holding's Renewed Motion for Jgm as a matter of Law [274-1] (erv) (Entered: 02/11/2002)
05/13/2002	275	MOTION by defendant (for order) to take judicial notice in support of renewed motion for judgment as a matter of law and in opposition to plas' motion for permanent injunction and rule 7.1 certification (pap) (Entered: 05/14/2002)
05/30/2002	276	Opposition (RESPONSE) by plaintiffs to dft's motion (for order) to take judicial notice in support of renewed motion for judgment as a matter of law and in opposition to plas' motion for permanent injunction [275-1] (pap) (Entered: 05/31/2002)
06/14/2002	277	REPLY by defendant Laboratory Corp Amer in support of motion (for order) to take judicial notice in support of renewed motion for judgment as a matter of law and in opposition to plas' motion for permanent injunction [275-1] (pap) (Entered: 06/17/2002)
11/20/2002	278	ORDER by Judge Zita L. Weinshienk: granting dft's motion for leave to file corrected memorandum in support of Laboratory Corporation of America Holding's renewed motion for jgm as a matter of law [274-1]; denying dft's motion for judgment as a matter of law [249-1]; denying dft's alternative motion for new trial [251-1]; denying dft's motion to alter or amend judgment [246-2],

[253-1]; denying dft's motion to take judicial notice in support of renewed motion for judgment as a matter of law and in opposition to plas' motion for permanent injunction [275-1]; granting plas' motion for enhanced damages and atty fees for willful infringement as to the enhanced damages to pla CTI in the amt of $1,019,365.01 and will be considered as to atty fees upon submission of an affidavit from csl [254-1], [254-2]; granting plas' motion for permanent injunction [255-1]; granting pla Metabolite Laboratories, Inc's motion to confirm prejudgment interest in the amt of $473,946.97 [256-1]; granting pla Competitive Technologies, Inc's motion for prejudgment interest in the amt of $132,264.27 [257-1]; finding dft's motion to stay execution pending disposition of post trial motions [248-1] denied as moot; and judgment will be amended to reflect the addl amounts above (cc: all counsel) ; entry date .: 11/20/02 (lam) (Entered: 11/20/2002)

11/20/2002 279 AMENDED JUDGMENT by Judge Zita L. Weinshienk: that judgment is entered in favor of plas Metabolite Laboratories, Inc. and Competitive Technologies and against dft Laboratory Corporation of America Holdings; that damages are awarded to pla Metabolite for dft LabCorp's breach of contract in the amt of $3,652,724.61; that damages are awarded to pla Competitive Technologies, Inc., due to dft LabCorp's infringement by inducement or by contributory infringement in the amt of

		$1,019,365.01; that pla Metabolite Laboratories, Inc. is awarded $437,946.97 in prejudgment interest; that pla Competitive Technologies,Inc. is awarded $132,264.27 in prejudgment interest; and post- judgment interest shall accrue at the legal rate of 2.23% per annum from the date of entry of judgment re: [278-1] order, [246-2] judgment, [242-1] verdict (cc: all counsel) ; entry date : 11/20/02 (lam) (Entered: 11/20/2002)
11/20/2002	280	Corrected (AMENDED) memorandum of law by defendant Laboratory Corp Amer in support of renewed motion for judgment as a matter of law [249-1] (lam) (Entered: 11/21/2002)
11/22/2002	281	Unopposed MOTION by defendant Laboratory Corp Amer for (order) suspension of permanent injunction through 11/26/02 and certificate of compliance with LR 7.1 (pap) (Entered: 11/26/2002)
11/26/2002	282	Emergency MOTION by defendant Laboratory Corp Amer for stay pending appeal, suspension of permanent injunction , and for (order) approval of supersedeas bond or other security and certificate of compliance with LR 7.1 (pap) Modified on 11/27/2002 (Entered: 11/27/2002)
11/26/2002	283	Opposition by plaintiffs to Labcorp's motion for stay pending appeal suspension of permanent injunction [282-1], motion for (order) approval of supersedeas bond or other security [282-2] (pap) Modified on 11/27/2002 (Entered: 11/27/2002)

11/26/2002	285	MOTION by defendant Laboratory Corp Amer for forthwith (to expedite) consideration of its emergency motion for stay pending appeal, suspension of permanent injunction and for approval of supersedeas bond or other security (pap) (Entered: 11/27/2002)
11/26/2002	286	ORDER by Judge Zita L. Weinshienk granting motion for (order) suspension of permanent injunction through 11/26/02 [281-1] (cc: all counsel) ; entry date : 11/27/02 (pap) (Entered: 11/27/2002)
11/26/2002	293	COURTROOM MINUTES by Judge Zita L. Weinshienk regarding [282-1] motion for stay pending appeal, suspension of permanent injunction; hearing continued until 11/27/02; Suppersedeas Bond for $6,578,527.00 approved; Stay is continued until further order of the Court ; entry date : 12/4/02 Court Reporter: Gwen Daniel (pap) (Entered: 12/04/2002)
11/27/2002	287	TRANSCRIPT of Further proceedings on 11/26/02 before Senior Judge Weinshienk (pages: 1-38) Prepared By: Gwen Daniel (certified copy) (pap) (Entered: 11/29/2002)
11/27/2002	288	NOTICE OF APPEAL TO FEDERAL CIRCUIT by defendant/counter-claimant Laboratory Corp Amer, re: judgment amend dated 11/20/02 [279-1], order [278-1] dated 11/20/02 and order dated 11/19/00 [118-1] ; Trancscript Purchase Order Form due 12/9/02 ; Notice mailed to all counscl on 11/29/02 Fee Status: $100 and $5 fee not paid (msn) Modified on 12/03/2002 (Entered: 11/29/2002)

11/27/2002	289	COURTROOM MINUTES by Judge Zita L. Weinshienk granting motion for stay pending appeal, suspension of permanent injunction [282-1] ; 6% royalties shall be paid on all future testing as to CTI until the ruling of the Federal Circuit; 21.5% royalties shall be paid on all future testing as to Metabolite; 6% royalties shall be paid on half the tests performed since the judgment in this case as to CTI; entry date : 11/29/02 Court Reporter: Gwen Daniel (pap) (Entered: 11/29/2002)
12/02/2002	290	$100.00 fee and $5.00 fee paid. Receipt No 239671. Court of Appeals Notified. appeal [288-1] (msn) (Entered: 12/02/2002)
12/02/2002	292	TRANSCRIPT of further proceedings on 11/27/02 before Judge Weinshienk (pages: 41) Prepared By: Gwen Daniel (certified copy)
12/05/2002	295	ORDER by Judge Zita L. Weinshienk granting motion for stay pending appeal, granting suspension of permanent injunction [282-1] with conditions, granting motion for (order) approval of supersedeas bond or other security [282-2] in the amount of $6,578,527.00 to be posted within days; denying as moot motion for forthwith (to expedite) consideration of its emergency motion for stay pending appeal, suspension of permanent injunction and for approval of supersedeas bond or other security [285-1] (cc: all counsel) ; entry date : 12/5/02 (pap) (Entered: 12/05/2002)

12/31/2002	305	REPORTER'S TRANSCRIPT of Trial to Jury on 11/05/01, Volume I, before Judge Weinshienk (Re: [288-1]) Pgs 1-185 Cert Copy Prepared By: Paul Zuckerman (msn) Modified on 01/02/2003 (Entered: 01/02/2003)
12/31/2002	306	REPORTER'S TRANSCRIPT of Trial to Jury on 11/6/01, Volume II, before Judge Weinshienk (Re: [288-1]) Pgs 186-389 Cert Copy Prepared By: Paul Zuckerman (msn) Modified on 01/02/2003 (Entered: 01/02/2003)
12/31/2002	307	REPORTER'S TRANSCRIPT of Trial to Jury on 11/7/01, Volume III, before Judge Weinshienk (Re: [288-1]) Pgs 390-593 Cert Copy Prepared By: Paul Zuckerman (msn) Modified on 01/02/2003 (Entered: 01/02/2003)
12/31/2002	308	REPORTER'S TRANSCRIPT of Trial to Jury on 11/8/01, Volume IV, before Judge Weinshienk (Re: [288-1]) Pgs 594-787 Cert Copy Prepared By: Paul Zuckerman (msn) Modified on 01/02/2003 (Entered: 01/02/2003)
12/31/2002	309	REPORTER'S TRANSCRIPT of Trial to Jury on 11/9/01, Volume V, before Judge Weinshienk (Re: [288-1]) Pgs 788-994 Cert Copy Prepared By: Paul Zuckerman (msn) Modified on 01/02/2003 (Entered:01/02/2003)
12/31/2002	310	REPORTER'S TRANSCRIPT of Trial to Jury on 11/13/01, Volume VI, before Judge Weinshienk (Re: [288-1]) Pgs 995-1200 Cert Copy Prepared By: Paul Zuckerman (msn) (Entered: 01/02/2003)

12/31/2002	311	REPORTER'S TRANSCRIPT of Trial to Jury on 11/14/01, Volume VII, before Judge Weinshienk (Re: [288-1]) Pgs 1201-1375 Cert Copy Prepared By: Paul Zuckerman (msn) (Entered: 01/02/2003)
12/31/2002	312	REPORTER'S TRANSCRIPT of Trial to Jury on 11/15/01, Volume VIII, before Judge Weinshienk (Re: [288-1]) Pgs 1376-1589 Cert Copy Prepared By: Paul Zuckerman (msn) (Entered: 01/02/2003)
12/31/2002	313	REPORTER'S TRANSCRIPT of Trial to Jury on 11/16/01, Volume IX, before Judge Weinshienk (Re: [288-1]) Pgs 1590-1733 Cert Copy Prepared By: Paul Zuckerman (msn) (Entered: 01/02/2003)
12/31/2002	314	REPORTER'S TRANSCRIPT of Trial to Jury on 11/19/01, Volume X, before Judge Weinshienk (Re: [288-1]) Pgs 1734-1857 Cert Copy Prepared By: Paul Zuckerman (msn) (Entered: 01/02/2003)
12/31/2002	315	REPORTER'S TRANSCRIPT of Trial to Jury on 11/20/01, Volume XI, before Judge Weinshienk (Re: [288-1]) Pgs 1858-1879 Cert Copy Prepared By: Paul Zuckerman (msn) (Entered: 01/02/2003)
01/13/2003	318	ORDER staying permanent injunction pending appeal by Judge Zita L. Weinshienk regarding [278-1] order (modifies orders entered at oral argument on 11/27/02) (cc: all counsel) ; entry date : 1/14/03 (pap) (Entered: 01/14/2003)
08/05/2003	334	Order and JUDGMENT re: Attorney Fees and Costs: by granting plas' motion for attorney fees for willful infringement [254-2], granting plas' motion for attorney fees [294-1] to the extent that plas

		CTI and Metabolite will be awarded $1,105,605.07 in reasonable attorney fees; denying dft's motion for order compelling plas to produce documentation reflecting allocation of payment of fees by and between Metabolite and CTI [316-1]; Granting plas' motion to review clerk's taxation of costs and dft will be taxed an additional $6,993 in costs, for a total of $25,906 (cc: all counsel) ; entry date : 8/5/03 (pap) (Entered: 08/05/2003)
09/03/2003		$100.00 fee and $5.00 fee paid. Receipt No 246012. re: appeal [335-1] (msn) (Entered: 09/04/2003)
09/03/2003	335	NOTICE OF APPEAL to the U.S. COURT OF APPEALS FOR THE FEDERAL CIRCUIT by Laboratory Corp Amer re: judgment filed 8/5/03 [334-1] and from all other orders incorporated by reference in or related in any way to the Court's 8/5/03 "Order and Judgment Re Attorney Fees and Costs," other than those orders that are already on appeal pursuant to the Notice of Appeal filed in this case on 11/27/03; Notice of transcript purchase order form due 9/15/03; Notice mailed to all counsel on 9/4/03 (msn) Modified on 09/04/2003 (Entered: 09/04/2003)
08/16/2004	342	MANDATE from the Federal Circuit Court of Appeals; CA # 03-1120; Dt issued 8/12/04; Judgment of 6/8/04 affirming the decision of the District Court on appeal [288-1] (djs) (Entered: 08/16/2004)
05/17/2005	395	JOINT MOTION to Stay Case until 7/5/05 pending the Supreme Court ruling

by Plaintiffs Metabolite Laboratories, Inc., Competitive Technologies, Inc., Defendant Laboratory Corporation of America Holdings. (pap,) (Entered: 05/18/2005)

05/18/2005 396 MINUTE ORDER granting [395] Joint Motion to Stay. Case is stayed until 7/5/05. Hearing set 5/19/05 is vacated. Joint status report due on or before 7/8/05. Entered by Judge Zita L. Weinshienk on 5/18/05. (pap,) (Entered: 05/19/2005)

07/18/2005 398 MINUTE ORDER re: [396] Order on Motion to Stay. Status Report due by 10/17/2005.Entered by Judge Zita L. Weinshienk on 7/18/05. (pap,) (Entered: 07/18/2005)

10/14/2005 399 MINUTE ORDER: the stay entered by the court on 5/18/05 is extended to 10/18/05. Status Report due by 10/18/2005 by Judge Zita L. Weinshienk on 10/14/05. (dlb,) (Entered: 10/14/2005)

10/24/2005 402 MINUTE ORDER Stay enter by 399 Order shall remain in effect until November 10, 2005. Joint Status Report due by 11/10/2005.Entered by Judge Zita L. Weinshienk on 10/24/05. (pap,) (Entered: 10/24/2005)

11/15/2005 404 MINUTE ORDER, It is ORDERED that the stay entered by the Court in the Minute Order filed on October 24, 2005, shall remain in effect until the U.S. Supreme Court issues a ruling on the issue described in the parties' November 10, 2005, Joint Status Report, absent further

order. Set Deadlines: Status Report due by 6/30/2006. by Judge Zita L. Weinshienk on 11/15/05. (erv,) (Entered: 11/15/2005)

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

Civil Action No. 99-Z-870

METABOLITE LABORATORIES, INC., *et al.*,

Plaintiffs,

vs.

LABORATORY CORPORATION OF AMERICA HOLDINGS,

Defendant.

REPORTER'S TRANSCRIPT
(Markman Hearing)

Proceedings before the HONORABLE ZITA L. WEINSHIENK, Judge, United States District Court for the District of Colorado, commencing at 10:18 a.m., on the 16th day of November, 2000, in Courtroom C-400, United States Courthouse, Denver, Colorado.

* * * *

[Page 6, line 22 to Page 9, line 13]

THE COURT: The word "correlating": From the claim language and the prosecution history, it must be a verb, not a noun; and that means to establish a mutual or reciprocal relationship between.

Let's see. "Deficiency." Did I cover that? Deficiency means—and this is based on the claim language and corroborated by the patent record. "Deficiency" means shortage of a substance necessary to health.

And it appears to me it does not and should not have the addition of words talking about hematologic or neuropsychiatric abnormalities.

So we've got detecting, deficiency, elevated, correlating. "Distinguishing" really comes in with Claim 18. If you want, we can talk about that. But I don't think it's probably necessary. It seems to me that it's pretty clear that it just means to separate into kinds, classes, or categories. And I don't think the parties are in dispute about that.

The problem arises with the word correlating. And we know from reading this brief and from reading the history and the fact that the Claim 13 was denied and then amended and the inventor was told to put in the steps—I'm trying to remember the language. Let me just get that.

Claim 13 was rejected because the homocysteine tests alone were already known in prior history and the inventor was told actually to put in—I think the language was discrete tests—steps. I don't have that right in front of me now, but we'll find it.

We know from case law going all the way back—

Okay. Here it is: "Patent examiner required a method involving discrete, sequential process steps." We know from that that "correlation" must be a verb and not a noun. It has to be an active step, because the assaying step is not sufficient. It's a statement.

But we know going all the way back in history, early cases, that an invention is not just an idea, it is not just a mental discovery. It must combine the idea with the means of putting it into practice and producing a desired result.

And so until the discovery is put into a practical form, there is no invention. There is no valid patent.

Let's see. The Supreme Court, way back when, in the *Symington* case said, "A conception of the mind, not represented in some physical form, is not an invention."

So if one takes the statement, which may very well be a wonderful new conception, that if there is an elevated level of total homocysteine and if that elevated level is correlated in body fluid with deficiency—can be correlated—that elevated level can be correlated in said body fluid with deficiency of cobalamin or folate, that is certainly a new idea, something original.

But what is the practicable—practical form of that? What are the actual steps? What are the discrete, sequential steps for putting into practice this new statement?

And I really have problems with that, quite frankly. And I'm not sure that that's a subject for today's hearing, which is a *Markman* hearing. But it certainly is something that we're going to have to talk about, because as wonderful as this thought is, unless there is some step, practicable step, and it's put into a practical form, then we don't have an invention. Statements are wonderful, but they're not inventions unless they're put into some sort of physical form or practical form.

And that's what I think the patent examiner was requiring. And I'm not quite sure how Claim 13 actually in the last state was approved, unless there is something that I'm not understanding—and I'm certainly not a scientist, as Dr. Allen is—as to how this statement, ingenious as it may be, can be put into a practical form.

* * * *

[Page 13, line 16 to Page 15, line 12]

MR. BEATON: Maybe I should focus on this word "correlating," which I think has troubled you with respect to what happened in the prosecution history. I think that has gotten a bit confused here.

As I read the prosecution history, the professors initially submitted Claim 13, stating that it was a method to detect a deficiency in cobalamin or folate by assaying for an elevated level of total homocysteine.

THE COURT: Okay.

MR. BEATON: So this idea of there being some sort of tie between the assay for elevated total homocysteine and a deficiency in folate or cobalamin was there right from the get-go.

Now, what the examiner came back and said was, I'm not so sure that you've really set this forth in discrete steps.

THE COURT: Exactly.

MR. BEATON: So the professors came back and said, Okay, let's take a step-by-step approach to this just to be clear. We've always said all along that there has to be something to do with deficiencies in vitamins. The claim did not cover, as it was initially filed, all total homocysteine tests. Never covered that. It doesn't cover that now. We don't so contend. There has to be this second step of correlating an elevated level of total homocysteine—excuse me—with deficiencies of at least one of the two vitamins.

THE COURT: And let me just interject. It appears to me that that step is covered in Claim 18.

MR. BEATON: Yes. Claim 18 goes a little bit further. It says: Not only will you correlate an elevated level of total homocysteine with deficiencies in the two vitamins, you'll figure out which of the two is deficient—

THE COURT: Right.

MR. BEATON: —by a separate assay for methylmalonic acid, MMA.

But in Claim 13, you don't have to figure out which of the two is deficient; you just have to assay for elevated levels of total homocysteine, which LabCorp has admitted that it does. And then the second step, which is the one in dispute, you have to correlate an elevated level of total homocysteine with a deficiency of cobalamin or folate. You don't have to say

which one. You just have to say at least one of them is deficient.

That's the step that was specifically added by the professors. That step is required.

THE COURT: And how do you put into practical application that second step? Because that's what's not clear to me or not clear from a reading of Claim 13.

* * * *

[Page 16, line 19 to Page 23, line 19]

THE COURT: Well, let me just ask you, because I'm not sure I'm understanding, and I do want to understand: Are you suggesting another step to 13?

MR. BEATON: No. There are two steps. There has to be an assay, which of course, is an affirmative act. That's more than an idea.

THE COURT: Okay. High homocysteine.

MR. BEATON: And there has to be a second step. Now, a person who just does an assay somehow armed with the knowledge—and this goes to your idea point, I think—that there is some sort of correlation between elevated homocysteine and deficiencies in the vitamin—that person may or may not infringe the patents. We don't need to answer that, because that's not this defendant.

There needs to be a second step. There needs to be this correlating. And that is done by this defendant, and he so admits with respect to the panel test; that the correlating as I mentioned constitutes the act of presenting the test results together with information showing this mutual or causal or parallel relationship, which is the definition of "correlate."

We got into this because we started on the question of extrinsic evidence, and I think that that extrinsic evidence of the defendant's specific admissions that they do correlate in

the panel test answers your question as to what in the real world does correlating look like.

THE COURT: And are you—is the plaintiff objecting to the—what appears to be really a plain meaning, a meaning derived from the language of the claim that "correlating" means to establish a mutual or reciprocal relationship?

MR. BEATON: No. We would agree that that is precisely the definition of correlating.

THE COURT: Okay.

MR. BEATON: And specifically, it does not require some sort of perfection, it does not require a medical diagnosis, it doesn't require a certain determination.

THE COURT: Does it require a practical form of ascertaining, of correlating?

MR. BEATON: I believe it requires something more than knowledge upstairs in the mind of somebody. It requires taking that homocysteine level that has been determined by an assay and comparing it against some sort of benchmark so that a person can make a judgment as to whether it's elevated to the point that there is a likelihood, not a certainty, but a likelihood of one of the two vitamin deficiencies.

If this case were—

THE COURT: Comparing it in somebody's mind, or comparing it with a practical test?

MR. BEATON: I think that there has to—there has to be more than just a mental step in someone's mind.

THE COURT: Right.

MR. BEATON: There needs to be—in my mind, at least—there needs to be something presented that shows this parallel, mutual, or reciprocal, or causal—whatever you want to call it—this relationship. Something needs to be presented showing that relationship.

THE COURT: I see that in Claim 18, but I don't in Claim 13. So where is it in Claim 13?

MR. BEATON: I believe it's in the word "correlating," and I believe that the patent office was fairly explicit in saying we want that set forth in a discrete sort of way.

THE COURT: Maybe you could just tell me, not a scientist, but tell me what practical steps are done to do that? Because we know from the case law that there must be a practical form. Can't be just a mental conception.

So what do you do? No. 1, No. 2, No. 3, No. 4. What do you do to correlate?

MR. BEATON: To answer that, maybe we should look at their directory of services which their patent attorney stated two years ago contains the correlating step in, and their Rule 30(b)(6) witness acknowledged the same in his deposition last winter. It's in Exhibit C to our opening Markman brief.

THE COURT: Well, who are you talking about, "they"? We're talking about plaintiff. Plaintiff is the one that has Claim 13. Every person—if Claim 13 is properly patented, it has two steps for every scientist, every person who uses it. Every person using this invention or method or practical invention uses it in the same way. How do they use it, using the word "correlating"? That's the problem I have with it.

I think it's hard for you to tell me that.

MR. BEATON: Well, the answer to the question is what—the answer to the question of what constitutes the correlate step, I think, is given by example in the LabCorp directory of services.

THE COURT: No, I don't think you can go to LabCorp.

I'm talking about the plaintiff, the patent. We can't look at what LabCorp does. You have to look at what the patent, what Claim 13 says.

MR. BEATON: Okay. You're interested in an example of the correlation occurring in the description of the patent?

THE COURT: No, I'm not interested in an example. I'm interested in what Claim 13 says you do.

MR. BEATON: Well, Claim 13 says you correlate your elevated homocysteine with a deficiency in one of the two vitamins.

THE COURT: Okay. And I want to know what the practical steps are for doing that.

MR. BEATON: Okay. First step is to assay for total homocysteine.

THE COURT: Well, we've done that. The first step, I don't have problems with.

MR. BEATON: Right. That results in a number.

The person takes that number and compares it against some sort of benchmark that he has. If it's above that benchmark, then he has some evidence that the total homocysteine is elevated. The patent teaches that that can be interpreted to mean that there is a deficiency in one of the two vitamins. And the data in the patent support that.

Now, if the person doesn't do that comparison—maybe this is what you're looking for, your Honor. The person needs to do a comparison. The person needs to compare the homocysteine result against a benchmark; and if it's elevated, then it correlates with a deficiency in the vitamins. If it's not elevated against that benchmark, then it doesn't.

Now, as you pointed out, the benchmark—

THE COURT: Well, I'm happy—that's the first step you're talking about. I'm asking you about the second step. The correlation. Because, indeed, it seems to me that has to be a step, it has to be a practical step, much as the first step, which is measuring the homocysteine to see if it's elevated.

MR. BEATON: I think you may be looking for a mechanical sort of step, where, for example, in the first step the laboratory does an assay.

There is no mechanical step here, and there need not be for the claim to be patentable. The step here indeed is a comparison step. That's perfectly fine under patent law. We don't need for there to be something like the homocysteine is mixed up with this or that and it turns blue.

THE COURT: Okay. What is the comparison?

MR. BEATON: The comparison is taking that homocysteine level determined by the first step and comparing it against some benchmark to determine whether it's elevated and hence correlates with vitamin deficiencies.

THE COURT: Hold on. Comparing it to see if it's elevated is the first step. I'm interested in the second step, because there has to be a second step, or at least I think there does because that's what the patent examiner said. There has to be discrete, sequential process steps.

I have no problem with whatever you do to find out you've got a homocysteine which is at an elevated level. And I think "elevated" pretty much means what we agreed on above the normal range, whether it's the normal range for a human or for an animal. And that can be determined.

But what is the second step? If you can just explain that to me so I can try to understand it, fine. Maybe this is something that only a scientist can understand, so tell me if that's the case.

MR. BEATON: Well, let me take another shot.

I think the second step is taking that homocysteine level that's been determined by the first step, comparing it against a benchmark chosen by the tester, which need not be 22 or any other particular benchmark but some benchmark and saying, aha, it's above that benchmark. Based on our data, which may be presented in a table, it may be presented in a

computer program, it may be presented in a variety of different ways, there is a likelihood—and here's the step—there is a likelihood of a vitamin deficiency, or conversely, there is not a likelihood of a vitamin deficiency.

THE COURT: Well, wasn't that the wording of Claim 13 before it was revoked or rejected and then amended?

MR. BEATON: I think it was close to that. But what it didn't do was set forth this correlating in a distinct step in the body of the claim. Instead, it was in the preamble of the claim. It read "A method for detecting a deficiency of cobalamin or folate in warm blooded animals by assaying a body fluid for an elevated level of total homocysteine."

The examiner said, Well, okay, you assay for an elevated level of total homocysteine, but what do you do with that—said the examiner.

The professors said well, we told you in the preamble what you do with that; but if you want us to put that in a distinct step in the body, fine. What you do is you take that total homocysteine level that you assayed for and you compare it with the benchmark to reach a determination, or a likelihood.

* * * *

[Page 29, line 1 to Page 31, line 4]

THE COURT: Okay. I understand what you're saying.

So what is it? Let's be very specific what you're saying, then, about that. You're talking about the second step, the correlation step.

MR. HIGGINS: Correct your Honor. The second step.

As that claim is written and in view of the prosecution history and specification, the correlating step requires a person to show that the elevated level of total homocysteine was caused by a deficiency of cobalamin or folate for that particular assay. That is the only way that claim can stake out a boundary where the—

THE COURT: Well, I don't see the words "caused by" in the patent.

MR. HIGGINS: Your Honor, the language, the interpretation of correlating, it says, "correlating is to establish a mutual or reciprocal relationship between."

THE COURT: Yes. Yes.

MR. HIGGINS: You think the step of correlating an elevated level with a deficiency—in other words, to correlate, you show or establish that the elevated level results are caused by the deficiency.

It says, "to show or establish," or you used the term "to establish" a mutual or reciprocal relationship between.

And without taking some active step to make that correlation or determination, then just an elevated level of total homocysteine falls within Claim 13, because based on the claim interpretation that Mr. Beaton and the plaintiffs have tried to present under claim interpretation, again, how does one know what assays for total homocysteine fall within Claim 13 and those that don't? Those prior art assays that were specifically noted by the examiner—

THE COURT: Well, if—it seems to me that the plain meaning of Claim 13 is that if you have this elevated level of homocysteine—in other words, above the normal range—and it depends, I guess, on which fluid you are testing and maybe which animal. I'm not as sure as you are that this is humans only, but perhaps it is.

MR. HIGGINS: No, your Honor, the claim does cover animals. But as far as the lawsuit goes—

THE COURT: Have you stipulated humans only?

MR. HIGGINS: LabCorp mainly does for humans.

THE COURT: Okay. So above the normal range. And it indicates that there might be this deficiency, and so you're

saying—you're saying that you have problems in seeing what the second step is or the active step.

MR. HIGGINS: That's correct, your Honor. Just indicating is not a step; it's not an active step.

Your Honor, for some extrinsic evidence from the—

THE COURT: You guys are the experts on patents. Can you patent a brilliant idea?

MR. HIGGINS: No, your Honor, you cannot patent an idea.

THE COURT: Because this may be a brilliant idea, and the question is: Is it patentable?

* * * *

[Page 34, line 24 to Page 35, line 14]

MR. HIGGINS: Again, for correlating, I don't know that we disagree with the Court's statement that correlating means to establish a mutual or reciprocal relationship between.

THE COURT: Okay.

MR. HIGGINS: But what does that mean? When we get to trial, the jury has the task of taking the claim as it's been construed and applying it to the conduct.

And so what does it mean to establish a mutual or reciprocal relationship between an elevated level of total homocysteine and a deficient—

THE COURT: You're assuming that this issue is going to get to the jury. I've indicated that I have problems with it as a matter of law. If, indeed, I'm not convinced that it meets the legal test of being a combination of an idea and a means of putting it into practice, it's never going to get to the jury.

* * * *

[Page 50, lines 4-19]

THE COURT: Now, if you show the homocysteine level that was determined by the assay in relation to that range and you explain the relationship between elevated homocysteine and the vitamin deficiencies, you have thereby performed a correlating of the two.

Again, it's probably an issue for another day.

THE COURT: Again, is that a mental step, or is that an actual, practical, physical step which is required for a valid patent?

MR. BEATON: Well, in the case of LabCorp, they actually do this in a physical way. They do present tables showing ranges and probabilities, and so on.

Now, whether a physician who does this in his office merely with the knowledge of the relationship upstairs in his mind would infringe the patent I think is another question that's not going to be in this case.

* * * *

[Page 59, line 18 to Page 60, line 2]

MR. JABLONSKI: I do think having heard the argument here today that you have identified in your opening comments precisely what the question is in this Step 2, and that is what is correlating. And you've said that that requires an active step.

And while Mr. Beaton has attempted to verbalize some active step, what he's really describing is simply the general knowledge. There is no active step done by LabCorp, and that's why there is no infringement here. And he has struggled mightily to respond to your question, but there is no response. That's the bottom line here.

* * * *

[Filed Nov. 29, 2000]

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

Civil Action No. 99-Z-870

METABOLITE LABORATORIES, INC.,
a Colorado corporation, and
COMPETITIVE TECHNOLOGIFS, INC.,
a Delaware corporation,

Plaintiffs,

v.

LABORATORY CORPORATION OF AMERICA
HOLDINGS d/b/a LABCORP,
a Delaware corporation,

Defendant.

ORDER

This matter was before the Court on November 15, 2000, for oral argument on the construction of terms in plaintiffs' U.S. Patent No. 4,940,658, specifically Claim 13. Claim 13 reads:

> A method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of:
>
> > assaying a body fluid for an elevated level of total homocysteine; and correlating an elevated level of total homocysteine in said body fluid with deficiency of cobalamin or folate.

(defendant's exhibit A, column 41, lines 58-65).

"[T]he court has the power and obligation to construe as a matter of law the meaning of language used in the patent

claim." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The court may not rely upon extrinsic evidence to construe a claim unless terms remain ambiguous after consideration of the intrinsic evidence, which includes the claim terms, the patent specification, and the prosecution history. *Vitrionics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996). If the claim language is clear on its face, consideration of the rest of the intrinsic evidence "is restricted to determining if a deviation from the clear language of the claim is justified." *Interactive Gift Express, Inc. v. Compuserve Incorp.*, 2000 WL 1644598 (Fed. Cir.) (November 3, 2000). This Court has relied on the prosecution history to construe a term where the patentee relinquished a potential claim construction in an amendment to the claim or in an argument to overcome or distinguish a reference. *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 979 (Fed. Cir. 1999).

The Court will construe the following terms: "detecting," "deficiency," "elevated," and "correlating." Based on the claim language, the word "detecting" is means "determining the existence of." In the context of the patent specification, the term does not mean that a deficiency in cobalamin or folate must be determined with 100% accuracy, however.

The word "deficiency" means "a shortage of a substance necessary to health." Although defendant argues that a physician logically would not perform the assay unless alerted to the possibility of a deficiency by some symptom, to construe the term to include a reference to a hematologic or neuropsychiatric abnormality would be improper. It would import a limitation from the specification that is not justified by the claim language or patent record. Throughout most of the patent specification, "deficiency" is used to denote a shortage of a necessary substance.

"Elevated" means "raised above the normal range." Construing the term to refer to a specific numeric range would not be consistent with the claim language. The normal range

depends both upon which body fluids are measured, and which animal is tested. The prosecution history indicates the patent examiner initially rejected Claim 13 because the applicant failed to include "quantitative language." (defendants' exhibit F, p. 3). However, the patent examiner was satisfied with the applicant's reference to the normal ranges for homocysteine in serum and urine at the time of the invention as described in the patent specification and with the applicant's explanation that "methods for determining such ranges are well-known in the art." (defendant's exhibit G, pp. 7-8).

The prosecution history indicates that the term "correlating" must be one of several "discrete, sequential process steps" and "[t]he final step should be clearly related to the preamble of the claim." (defendant's exhibit F, p. 3). The patent examiner initially rejected Claim 13 because it appeared to patent a simple homocysteine test, which is known in prior art, and the preamble did nothing more than suggest an intended use for the homocysteine test. (defendant's exhibit H, p. 2). Therefore, the term is construed as meaning "to establish a mutual or reciprocal relationship between." "Correlating" is a verb, and must mean more than the simple existence of a relationship between a high level of homocysteine and a deficiency in cobalamin or folate. It must comprise a discrete, sequential process step, as suggested by the patent examiner.

The Court rejects defendant's argument that "correlating" is limited by the language of Claim 13 to correlation with hematologic or neuropsychiatric symptoms in order to confirm a deficiency in cobalamin or folate. Defendant's definition is derived from a non-limiting example, (defendant's exhibit A, column 10, line 25 - column 12, line 7), that described a study done by applicant Dr. Robert Allen in which the homocysteine test was used to confirm cobalamin folate deficiencies in patients displaying hematologic or neuropsychiatric symptoms. The study was included in the patent specification as an example of one potential use of the

applicant's discovery. Defendant's construction would read a limitation into the claim that would not be consistent with the term "correlating" as it is used throughout the patent specification.

The terms "detecting," "deficiency" and "elevated" in Claim 18 are construed as they are in Claim 13. Accordingly, it is

ORDERED that the term "detecting" in Claim 13 is construed to mean "determining the existence of." It is

FURTHER ORDERED that the term "deficiency" in Claim 13 is construed to mean "a shortage of a substance necessary to health." It is

FURTHER ORDERED that the term "elevated" in Claim 13 is construed to mean "raised above the normal range." It is

FURTHER ORDERED that the term "correlating" in Claim 13 is a verb that is construed to mean "to establish a mutual or reciprocal relationship between," and that describes a discrete step in a sequential process.

DATED at Denver, Colorado, this 29 of November, 2000.

BY THE COURT:

/s/ Zita L. Weinshienk
ZITA L. WEINSHIENK, Senior Judge
United States District Court

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

Civil Action No. 99-Z-870

METABOLITE LABORATORIES, INC., *et al.*,

Plaintiffs,

vs.

LABORATORY CORPORATION
OF AMERICA HOLDINGS,

Defendant.

REPORTER'S TRANSCRIPT
(Hearing on Motions for Summary Judgment)

Proceedings before the HONORABLE ZITA L. WEINSHIENK, Judge, United States District Court for the District of Colorado, commencing at 9:20 a.m., on the 1st day of March, 2001, in Courtroom C-400, United States Courthouse, Denver, Colorado.

* * * *

[Page 10, lines 3-21]

THE COURT: You know, we've talked about this before. The claim has to describe an invention in a way that allows people who read it to understand the scope. It has to do something. I think we've gone over this before. That's the problem. There has to be notice or an explanation to people. And you're saying it's there.

MR. BEATON: I am saying it's there. If I may, I can point you to the place in the—places in the patent specification that describe this step. I have—

THE COURT: Well, Claim 13, it would appear to me—and I could be wrong; I'm not a scientist, certainly—does not describe a correlating step except for what we've talked about, this mental understanding that there is a correlation between the high homocysteine and one of these two vitamins. What is the step?

MR. BEATON: The step is establishing the mutual relationship, and that is done in the patent by the presentation of evidence of the relationship between elevated homocysteine and the vitamin deficiencies.

* * * *

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

Civil Action No. 99-Z-870

METABOLITE LABORATORIES, INC.
a Colorado corporation,
and COMPETITIVE TECHNOLOGIES, INC.,
a Delaware corporation,

Plaintiffs,

vs.

LABORATORY CORPORATION OF
AMERICA HOLDINGS
d/b/a LABCORP, a Delaware corporation,

Defendant.

LABORATORY CORPORATION OF AMERICA HOLDINGS' ANSWER AND COUNTERCLAIMS TO FOURTH AMENDED COMPLAINT

Filed October 2, 2001

Defendant Laboratory Corporation of America Holdings ("LabCorp") responds to the allegations contained in plaintiffs' Fourth Amended Complaint and Jury Demand as follows:

* * * *

16. LabCorp admits that the '658 patent includes at least one claim which states: "A method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of: assaying a body fluid for an elevated level of total homocysteine and correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate." LabCorp further admits that the '658 patent includes independent claims 13 and 18 and that plaintiffs

have asserted these claims against LabCorp, and that the Court has held on summary judgment that claim 13 does not directly cover LabCorp's performance of the single homocysteine test (706994). Except as expressly admitted, the allegations of paragraph 16 are denied.

17. LabCorp admits that test 706960 is performed by LabCorp and the test results of homocysteine, methylmalonic acid, 2-methylcitric acid, and cystathianine are communicated to the physician along with information from which these results may be correlated with the presence or absence of deficiencies of cobalamin or folate. Except as expressly admitted, allegations of paragraph 17 are denied.

* * * *

FIRST AFFIRMATIVE DEFENSE

224. LabCorp has not infringed, induced, or contributed to the infringement of U.S. Patent No. 4,940,658 ("the '658 patent") because Plaintiff Metabolite has licensed LabCorp under the '658 patent, which license has not been terminated.

SECOND AFFIRMATIVE DEFENSE

225. In view of the history of the prosecution of the application resulting in the '658 patent, and the cancellation of claims and amendments made during prosecution of said application, the '658 patent as finally allowed may not be properly interpreted to read upon or include any assays for homocysteine used, offered for sale, or sold by LabCorp on which LabCorp has not paid royalties. Furthermore, plaintiffs are estopped by virtue of the doctrine of prosecution history estoppel (including but not limited to amendments and representations made to the United States Patent and Trademark Office specifically in order to distinguish the prior art and to obtain the patents) to rely on the doctrine of equivalents in order to obtain the scope for the patent as broader than the language of the claims.

THIRD AFFIRMATIVE DEFENSE

226. The '658 patent is invalid, unenforceable, and/or void for failure to comply with 35 U.S.C. §§ 102, 103, and 112. Claim 1 and dependent claims, claim 13 and dependent claims and claim 18 and dependent claims of the '658 patent are invalid under 35 U.S.C. § 103 in view of, but not limited to, material prior art and other information which indicates that the alleged invention that is the subject of the '658 patent would have been at least obvious to a person of ordinary skill in the art at the time the alleged invention was made. Claims 13 and 18 and their dependent claims are invalid under 35 U.S.C. § 112 ¶¶ 1&2 for insufficient written description and nonenablement. Claims 13 and 33 are invalid under 35 U.S.C. § 102(b) because the alleged invention claimed therein was disclosed in Refsum et al. (1985).

FOURTH AFFIRMATIVE DEFENSE

227. LabCorp has not contributorily infringed the '658 patent. The assays for homocysteine performed by LabCorp, on which royalties have not and are not being paid, are a staple article or a commodity of commerce suitable for substantial non-infringing use. LabCorp does not know that assays for homocysteine are especially made or especially adapted for use in an infringement of the '658 patent.

FIFTH AFFIRMATIVE DEFENSE

228. The plaintiffs have misused the '658 patent by over-broadly and impermissibly construing its claims to cover assays for homocysteine not falling within any claim of the '658 patent and asserting the '658 patent against those who perform assays for homocysteine that do not fall within any claim of the '658 patent so as to cause anticompetitive effect. Plaintiffs know that LabCorp and others perform homocysteine assays using a competitive enzyme immunoassay that is not covered by any claim of the '658 patent. Plaintiffs know that it is not good medical practice to use a single assay of homocysteine to determine deficiencies in cobalamin or folate. Plaintiffs know that LabCorp and others do not

correlate assays for homocysteine with deficiencies of cobalamin or folate. Yet, plaintiffs continue to assert the '658 patent against LabCorp and others who use the competitive enzyme immunoassay. Furthermore, Plaintiffs have knowingly and intentionally used the '658 patent to obtain royalties on assays that are not covered by the '658 patent. The '658 patent is unenforceable as a result of plaintiffs' misuse of the patent.

SIXTH AFFIRMATIVE DEFENSE

229. The '658 patent is invalid in view of the inequitable conduct committed during the prosecution of the application that led to the issuance of the '658 patent. Applicants filed the application leading to the issuance of the '658 patent without disclosing and providing to the Patent Examiner information of which they were aware that was material to the patentability of the inventions claimed in the application, including but not limited to Kang (1979), Wilcken (1981), Rosenberg (1983), and Brattstrom (1984). Additionally, applicants did not file an information disclosure statement and provide copies of prior art until almost two and one half years after filing the application and after the Patent Examiner had issued the first Office Action, and after the applicants had filed their first amendment arguing that: (1) "it was not previously known that elevated levels of homocysteine correlate with cobalamin and folate deficiency, nor was it suggested to use assays of total homocysteine and methylmalonic acid to diagnose and distinguish between these deficiencies," and (2) Mudd (1969) did not support the Patent Examiner's obviousness argument because the infant who had elevated levels of homocysteine had normal B12 levels and was therefore not suffering from a B12 deficiency. At the time applicants made those statements to the Patent Examiner, applicants had not provided the Examiner with copies of the material prior art. Applicants later provided the Patent Examiner with some prior art, but withheld articles by Wilcken, Rosenberg, Brattstrom, and others and buried a two-page Hoey article in over 500 pages of publications, a

significant number which were not prior art nor were particularly material to patentability. The prior art articles that applicants withheld were material to the patentability of plaintiffs alleged invention. Applicants did not point out the prior art that contradicted their earlier statements to the Patent Examiner so that the Patent Examiner would allow the '658 patent to issue. Also, in response to the Patent Examiner's rejection of claims 1-12 under 35 U.S.C. § 103 for obviousness, applicants made arguments that were contrary to what the prior art taught and did not provide the Examiner with the material prior art of which they were aware, including Kang (1979). Kang taught the step of claim 1 of adding a reducing agent such as 2-mercaptoethanol to a sample to be measured for total homocysteine. Applicants were aware of Wilcken, Rosenberg, Brattstrom (1984) and Kang (1979) because Allen and Stabler had cited these articles in their publications prior to the issuance of the '658 patent. Applicants withheld this material information with the intent to deceive the Patent Examiner in allowing the claims of the '658 patent to issue.

SEVENTH AFFIRMATIVE DEFENSE

230. Plaintiffs' claims for breach of contract and fraud which arose prior to the applicable statute of limitations period or which plaintiffs knew of or reasonably should have known of prior to the applicable statute of limitations period are barred by the statute of limitations.

EIGHTH AFFIRMATIVE DEFENSE

231. Plaintiffs' claims for breach of contract are barred by laches, waiver or estoppel. With respect to LabCorp's alleged breach for failing to certify royalty reports, plaintiffs have accepted LabCorp's royalty reports and payments for more than eight years without complaint and knew or should have known that the reports were not certified by an officer of LabCorp. LabCorp has relied on plaintiffs' acceptance of these reports and requiring certification of prior reports would be an undue burden. Plaintiffs claims for any unpaid

royalties going back more than two years from the date of this Fourth Amended Complaint are also barred by waiver, laches or estoppel in view of Article 3.03 of the Agreement which only requires LabCorp to maintain records pertaining to each royalty period for only two years in sufficient detail to permit the determination of royalties payable under the Agreement. Plaintiffs have unduly delayed in asserting claims for alleged past unpaid royalties.

NINTH AFFIRMATIVE DEFENSE

232. Metabolite's claims for copyright infringement are barred by the statute of limitations, 17 U.S.C. § 507.

TENTH AFFIRMATIVE DEFENSE

233. Metabolite impliedly, if not expressly, licensed LabCorp to use Metabolite's alleged copyrighted works.

ELEVENTH AFFIRMATIVE DEFENSE

234. Any use by LabCorp of Metabolite's alleged copyrighted works was and is a fair use.

TWELFTH AFFIRMATIVE DEFENSE

235. Metabolite has breached its duty of good faith and fair dealing under the Agreement and, therefore has materially breached the Agreement, by filing and maintaining this action against LabCorp, including Metabolite's assertion claims of breach of contract, patent infringement, copyright infringement, and fraud against LabCorp.

THIRTEENTH AFFIRMATIVE DEFENSE

236. Factual statements in Plaintiff Metabolite's patient report are not copyrightable subject matter.

FOURTEENTH AFFIRMATIVE DEFENSE

237. Plaintiffs' claims for breach of contract relating to any untimely payments for Licensed Assays for the NHL laboratories of LabCorp or for untimely payments for test no. 706994 prior to 1998 are barred by accord and satisfaction, or alternatively compromise and settlement, because Lab-

Corp has paid and Plaintiffs have accepted payment for those Licensed Assays.

FIRST COUNTERCLAIM
(DECLARATORY JUDGMENT OF NONINFRINGEMENT)

238. Upon information and belief, plaintiff Metabolite Laboratories, Inc. ("Metabolite") is a Colorado corporation having a place of business in Denver, Colorado.

239. Upon information and belief, plaintiff Competitive Technologies, Inc. ("CTI") is a Delaware corporation having a place of business in Fairfield, CT and owns or has owned U.S. Patent No. 4,940,658.

240. This claim is pursuant to the Federal Declaratory Judgment Act, 28 U.S.C. § 1331 for a declaratory judgment that LabCorp has not infringed and does not infringe any valid claim of the '658 patent, that the '658 patent is invalid and/or unenforceable and that LabCorp has not breached the Agreement with Metabolite.

241. This Court has jurisdiction over the parties to this counterclaim, all of who are presently parties to this litigation, pursuant to 28 U.S.C. §§ 1131 and 1338. The amount in controversy exceeds the sum of $75,000.00, exclusive of the interests and costs. Venue is appropriate in this forum.

242. There is an actual and justiciable controversy between the parties concerning the infringement, validity and/or enforceability of the '658 patent arising under the Patent Act, 35 U.S.C. §1 et. seq.

243. Prior to November 20, 1985, Clinical Chemistry published an article by H. Refsum et al which taught one of ordinary skill in the art a suitable method for use in determining levels of the total amount of homocysteine present in both free and complex forms in urine or blood of humans.

244. In 1969, Dr. McCully proposed that some form of homocysteine was involved in the pathogenesis of vascular disease, including coronary heart disease.

245. In 1969, The Lancet published a letter by J.G. Hollowell et al. which correlated a deficiency of cobalamin in a patient with elevated levels of homocysteine and cysteine-homocysteine mixed disulfide in the patient's urine. Hollowell et al also suggested in the letter that above normal levels of homocystine may be due to vitamin B_{12} deficiency.

246. In 1977, The American Journal of the Medical Sciences published an article by A.J. Greico which recommended routine screening of urine for homocystine as an important step in the prevention of accelerated atherosclerosis and occlusive vascular disease.

247. In 1982, the Journal of the Royal Society of Medicine published an article by Hoey et al. which taught that deficiencies of cobalamin result in abnormally raised levels of homocystine and the homocysteine-cysteine mixed disulphide.

248. In 1982, the Journal of the Royal Society of Medicine published an article by Hoey et al. which taught that assays of methylmalonic acid and assays of components of total homocysteine ("total homocysteine" as defined by the '658 patent), homocystine and the cysteine-homocysteine mixed disulphide, are useful in detecting deficiencies of cobalamin result in abnormally raised levels of homocystine and the homocysteine-cysteine mixed disulphide.

249. In 1984, Stroke published an article by Brattstrom et al. which showed that folic acid lowers plasma homocysteine in humans.

250. Prior to November 20, 1985, Metabolism published an article by Brattstrom et al. which suggests homocysteine or its derivatives might be worth considering as a risk factor for vascular disease and that folic acid therapy might be an effective prophylactic.

251. Prior to November 20, 1985, physicians had prescribed folic acid as a treatment for their patients who were diagnosed with diseases or inherited defects based on results of assays that determined the level of homocysteine in the patients' blood.

252. Prior to November 20, 1985, a person of ordinary skill in the art would have known and understood that assays for total homocysteine described in the 1985 Refsum et al. article published in Clinical Chemistry assist in determining deficiencies in cobalamin or folate.

253. Prior to November 20, 1985, physicians prescribed folic acid as a treatment for their patients who were diagnosed with deficiencies of folate based on results of assays that determined the level of homocystine and/or cysteine-homocysteine mixed disulfide in the patients' blood or urine.

254. Prior to November 20, 1985, physicians prescribed cobalamin as a treatment for their patients who were diagnosed with deficiencies of cobalamin based on results of assays that determined the level of homocystine and/or cysteine-homocysteine mixed disulfide in the patients' blood or urine.

255. As originally filed, the application, which issued as the '658 patent, contained claim 13 which did not include a step of "correlating an elevated level of total homocysteine in a body fluid of warm-blooded animals with a deficiency of cobalamin or folate."

256. In response to a rejection from the patent examiner of unpatentability over prior art, the named inventors of the '658 patent amended originally filed claim 13 to add the step of "correlating an elevated level of total homocysteine in a body fluid of warm-blooded animals with a deficiency of cobalamin or folate."

257. The only assays performed by LabCorp which plaintiffs accuse of infringing the '658 patent are the assays performed as test nos. 706994, 374983, and 716290.

258. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which plaintiffs accuse of infringing the '658 patent, do not include the step of combining a sample containing homocysteine with an internal reference standard comprising a known amount of homocysteine, labeled with a suitable marker.

259. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which plaintiffs accuse of infringing the '658 patent, do not include the step of adding sufficient reducing agent to insure randomization of the labeled and unlabelled homocysteine present in the sample.

260. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which plaintiffs accuse of infringing the '658 patent, do not include the step of measuring the relative amounts of labeled and unlabelled homocysteine with a mass spectrometer.

261. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which plaintiffs accuse of infringing the '658 patent, do not include the step of calculating the ratio of labeled to unlabeled homocysteine present in the sample.

262. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which plaintiffs accuse of infringing the '658 patent, do not include the step of deriving the amount of unlabeled homocysteine present in the sample.

263. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which the plaintiffs accuse of infringing the '658 patent, do not include any step that is equivalent to the step of combining a sample containing homocysteine with an internal reference standard comprising a known amount of homocysteine, labeled with a suitable marker.

264. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which the plaintiffs accuse of infringing the '658 patent, do not include any step that is equivalent to the step of adding sufficient reducing agent to insure randomization of the labeled and unlabeled homocysteine present in the sample.

265. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which the plaintiffs accuse of infringing the '658 patent, do not include any step that is equivalent to the step of measuring the relative amounts of labeled and unlabeled homocysteine with a mass spectrometer.

266. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which the plaintiffs accuse of infringing the '658 patent, do not include any step that is equivalent to the step of calculating the ratio of labeled to unlabelled homocysteine present in the sample.

267. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which the plaintiffs accuse of infringing the '658 patent, do not include any step that is equivalent to the step of deriving the amount of unlabelled homocysteine present in the sample.

268. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which the plaintiffs accuse of infringing the '658 patent, do not include any step of correlating an elevated level of total homocysteine in a body fluid with a deficiency of cobalamin or folate.

269. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which the plaintiffs accuse of infringing the '658 patent, do not include any step that is equivalent to the step

of correlating an elevated level of total homocysteine in a body fluid with a deficiency of cobalamin or folate.

270. LabCorp does not encourage others to use the assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method, which plaintiffs accuse of infringing the '658 patent, to correlate an elevated level of total homocysteine determined by the assay with a deficiency of cobalamin or folate.

271. The assays for total homocysteine performed by LabCorp as test no. 706994 using Abbott's immunoassay method on which royalties have not and are not being paid do not infringe any valid claim of the '658 patent and are not covered by any valid claim of the '658 patent.

272. As a direct and proximate result of plaintiffs' assertion of the '658 patent against LabCorp, LabCorp has suffered irreparable damages, including but not limited to injury to its reputation and good will in an amount that cannot be ascertained and which cannot be adequately compensated by monetary relief alone.

273. The damage or injury to LabCorp is continuing and will continue until enjoined by this Court.

274. Upon information and belief, plaintiffs' actions in wrongfully asserting the infringement claim have been and are knowing and willful.

SECOND COUNTERCLAIM
(DECLARATORY JUDGMENT OF INVALIDITY)

275. Paragraphs 238-254, above, are incorporated herein by reference.

276. The claims of the '658 patent are invalid for failure to comply with the following requirements of the Patent Act, 35 U.S.C. § 1 et seq., 35 U.S.C. §§ 102(b), 103(a) and 112 ¶¶ 1&2.

277. Claims 1 and dependent claims are invalid under 35 U.S.C. § 103 for being obvious in view of Marcela et al.,

Anal. Biochem. (1985) 150:58-66 and Kang et al., Pediatric Research, Vol. 13, pp. 1141-43 (1979) or Saetre/Rabenstein (1978). Marcell teaches the method of claim 1 without the step of adding the reducing agent and Kang et al teaches the specific reducing step of claim 1. Dependent claims 2-12 are also obvious because they recite insubstantial elements that are also obvious to one of ordinary skill in view of Marcell, Saetre/Rabenstein, and Kang et al.

278. Claims 13 and 33 of the '658 patent are invalid under 35 U.S.C. § 102(b) based on Refsum et al., Clin. Chem. Vol. 31, No.4 (1985) because Refsum et al teach a method for assaying for total homocysteine and suggest using such method to determine diseases in humans relating to homocysteine metabolism. A person of ordinary skill in the art would have known before November 20, 1985 that such diseases included cobalamin or folate deficiency.

279. Claims 13 and dependent claims of the '658 patent are invalid under 35 U.S.C. § 103 as being obvious over the prior art including anyone of the following publications (Trugman et al. (1985) or Greico et al. (1977) or Higginbottom et al. (1978) or Hoey et al. (1982) or Hollowell et al. (1969) or Mudd (1969), or Bevan (1982) or Freeman et al (1975) or Trugman et al. (1985) in view of Saetre/Rabenstein (1978) or Refsum et al. (1985).

280. Claims 13 and dependent claims are also invalid under 35 U.S.C. § 112 ¶ 1 because the specification does not contain a sufficient written description or enable one of ordinary skill in the art to practice the claimed invention, which requires the steps of assaying for an elevated level of total homocysteine and correlating the elevated level of total homocysteine with a deficiency of cobalamin or folate. Total homocysteine can be elevated for a number of reasons, including renal diseases, B_6 deficiency, inherited disorders of metabolism, thyroid hormone deficiency, and the effects of certain common drugs, including cancer drugs.

281. Claims 13 and dependent claims are also invalid under 35 U.S.C. § 112 ¶ 2 because the claims do not particularly point out and distinctly claim the subject matter which Allen et al. regard as their invention. Because homocysteine can be elevated for a number of reasons other than a deficiency of cobalamin or folate and because a person may be deficient in cobalamin or folate and not have an elevated level of total homocysteine, one of ordinary skill cannot simply assay for an elevated level of total homocysteine and then correlate with a deficiency of cobalamin or folate.

282. Claims 18 and dependent claims are invalid under 35 U.S.C. § 103 as being obvious over the prior art including Hollowell et al. (1969), Hoey et al. (1982) or Higginbottom et al. (1978) or Trugman et al (1985) in view of Refsum et al. (1985). Hollowell, Hoey and Higginbottom teach the use of assays for homocysteine and methylmalonic acid together to determine deficiencies in cobalamin or folate. Refsum et al teaches a method for assay total homocysteine and teaches its use for determining diseases involving homocysteine metabolism, which include cobalamin and folate deficiencies. Norman (1982) teaches use of assays of methylmalonic acid to determining deficiencies in cobalamin.

283. Claims 18 and dependent claims are also invalid under 35 U.S.C. § 112 ¶ 1 and 2 because assays for homocysteine and methylmalonic acid cannot distinguish between deficiencies of cobalamin or folate because if both homocysteine and methylmalonic acid are elevated, then a deficiency of cobalamin or cobalamin and folate may exist. Also, homocysteine can be elevated for reasons other than deficiencies of cobalamin or folate and methylmalonic acid may be elevated for reasons other than cobalamin deficiency so that assays of total homocysteine and methylmalonic acid cannot be used to detect and distinguish between deficiencies of cobalamin or folate or both.

284. As a direct and proximate result of plaintiffs' assertion of the '658 patent against LabCorp, LabCorp has suffered irreparable damages, including but not limited to injury

to its reputation and good will in an amount that cannot be ascertained and which cannot be adequately compensated by monetary relief alone.

285. The damage or injury to LabCorp is continuing and will continue until enjoined by this Court.

286. Upon information and belief, plaintiffs' actions in wrongfully asserting this lawsuit have been and are knowing and willful.

THIRD COUNTERCLAIM
(DECLARATORY JUDGMENT OF PATENT MISUSE)

287. Paragraphs 238-286 above, are incorporated herein by reference.

288. The plaintiffs have misused the '658 patent by over-broadly and impermissibly construing its claims to cover assays for homocysteine not falling within any claim of the '658 patent and asserting the '658 patent against LabCorp and others who perform assays for total homocysteine that do not fall within any claim of the '658 patent so as to cause anticompetitive effect. Plaintiffs have used the '658 patent to require LabCorp and others to pay royalties on assays that are not covered by the '658 patent.

289. Upon information and belief, before asserting the '658 patent against LabCorp and others, plaintiffs knew that, prior to November 20, 1985, doctors used the results of assays of total homocysteine, including elevated levels of total homocysteine, to diagnose or treat certain diseases or inherited defects in their patients.

290. Upon information and belief, before asserting the '658 patent against LabCorp and others, plaintiffs knew that, prior to the alleged invention by the named inventors of the methods claimed in the '658 patent, doctors used the results of assays of total homocysteine, including elevated levels of total homocysteine, to diagnose or treat certain diseases or inherited defects in their patients.

291. Upon information and belief, before asserting the '658 patent against LabCorp and others, plaintiffs knew that, prior to November 20, 1985, doctors had prescribed folic acid as a treatment for their patients who were diagnosed with diseases or inherited defects based on results of assays that determined the level of homocysteine, including elevated levels of homocysteine, in the patients' blood.

292. Upon information and belief, before asserting the '658 patent against LabCorp and others, plaintiffs knew that, prior to the alleged invention by the named inventors of the methods claimed in the '658 patent, doctors had prescribed folic acid as a treatment for their patients who were diagnosed with diseases or inherited defects based on results of assays that determined the level of homocysteine, including elevated levels of homocysteine, in the patients' blood.

293. Upon information and belief, before asserting the '658 patent against LabCorp and others, plaintiffs knew that, prior to November 20, 1985, doctors had prescribed cobalamin (vitamin B12) as a treatment for their patients who were diagnosed with diseases or inherited defects based on results of assays that determined the level of homocysteine, including elevated levels of homocysteine, in the patients' blood.

294. Upon information and belief, before asserting the '658 patent against LabCorp and others, plaintiffs knew that, prior to the alleged invention by the named inventors of the methods claimed in the '658 patent, doctors had prescribed cobalamin (vitamin B12) as a treatment for their patients who were diagnosed with diseases or inherited defects based on the results of assays of homocysteine that determined the level of homocysteine, including elevated levels of homocysteine, in the patients' blood.

295. Plaintiffs know that LabCorp and others perform assays for total homocysteine using a competitive enzyme immunoassay that is not covered by any claim of the '658 patent.

296. Plaintiffs know that it is not good medical practice to use a single assay of homocysteine to determine deficiencies of cobalamin or folate.

297. Plaintiffs know that the results of more than 50 percent of the assays of total homocysteine do not yield an elevated level of total homocysteine.

298. Plaintiffs know that LabCorp and other laboratories do not correlate assays for total homocysteine with deficiencies of cobalamin or folate. Yet, plaintiffs continue to assert the '658 patent against LabCorp who uses the competitive enzyme immunoassay to assay levels of total homocysteine.

299. Plaintiff CTI has demand and received royalties from laboratories who perform single homocysteine assays not using a gas chromatography/mass spectrometry method and which do not correlate an elevated level of total homocysteine with a deficiency of cobalamin or folate.

300. Plaintiff CTI has demanded and received from at least one clinical laboratory royalties on single homocysteine assays which are not performed using gas chromatography and mass spectrometry and which do not yield an elevated level of total homocysteine.

301. Plaintiffs demand that LabCorp pay plaintiffs royalties on each single homocysteine test (706994) performed using Abbott's immunoassay method.

302. The '658 patent is unenforceable as a result of plaintiffs' misuse of the patent.

303. As a direct and proximate result of plaintiffs' assertion of the '658 patent against LabCorp, LabCorp has suffered irreparable damages, including but not limited to injury to its reputation and good will in an amount that cannot be ascertained and which cannot be adequately compensated by monetary relief alone.

304. The damage or injury to LabCorp is continuing and will continue until enjoined by this Court.

305. Upon information and belief, plaintiffs' actions in bringing this lawsuit to recovery royalties to which they are not entitled have been and are knowing and willful.

PRAYER FOR RELIEF

WHEREFORE, LabCorp prays the Court grant it the following relief, including:

A. Judgment dismissing, with prejudice, plaintiffs' Complaint;

B. A declaration that LabCorp has not infringed or contributed to infringement of any valid claim of the '658 patent, that the patent is invalid and/or unenforceable and that the Agreement is void and unenforceable;

C. A declaration that plaintiffs have misused the '658 patent and that the '658 patent is unenforceable.

D. An injunction enjoining plaintiffs and any parties in active concert therewith from asserting the patent or instituting or prosecuting any lawsuit or other legal proceeding seeking in any way to enforce or maintain the '658 patent against LabCorp or its customers;

E. That this case be declared exceptional within the meaning of the Patent Act, 35 U.S.C. § 285, and that LabCorp be awarded its costs and reasonable attorneys' fees incurred in connection with the matter;

F. An award of attorneys' fees and costs under 17 U.S.C. § 505.

G. That all issues of fact be tried by a jury; and

H. Such other and further relief as the Court may deem just and proper.

Respectfully submitted this 1st day of October, 2001.

/s/ John P. Higgins

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

Civil Action No. 99-z-870

METABOLITE LABORATORIES, INC., et al.,

Plaintiffs,

vs.

LABORATORY CORPORATION
OF AMERICA HOLDINGS,

Defendant.

REPORTER'S [TRIAL] TRANSCRIPT

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Voir Dire Examination of Prospective Jurors

[Page 75, lines 3-7]

MR. JABLONSKI [Counsel for LabCorp]: * * * And this is a very impressive jury, very well-educated.

THE COURT: Tremendously. * * *

* * * *

Dr. Sally Stabler—Direct

[Page 180, line 3 to Page 182, line 5]

BY MR. WHITEHAIR:

Q. Have you had occasion to make a list of the traits that you desire when you're investigating a potential diagnostic test?

A. I did.

Q. Did you prepare a list?

A. I did.

Q. Let me have you turn to the small notebook, the very first document, Exhibit Demo 1.

MR. WHITEHAIR: And this, for the record, is a demonstrative. And I believe your Honor has already explained that these won't go back to the jury room.

THE COURT: All right.

BY MR. WHITEHAIR:

Q. We have it open in front of us. Are you going to be—

A. Unfortunately, Dr. Stabler doesn't.

All right.

Q. Before we look at it, what generally were you trying to capture in putting together a list of traits?

A. These are all the things that go in your mind when you actually think about a test that could be a good test diagnostically. If you were to write a manuscript about what you did, these are the kind of points that the referees would expect you to sort of address; that yeah, this would be a good thing, this would work.

Q. All right. Let's just start through. And you directed all the contents of this document. Right. This is your work?

A. Yeah.

Q. No. 1, readily found.

A. Well, it has to be easy to measure, and it needs to be in something you can get easily. And that would be blood and urine.

Q. What are some other options that are hard—

A. Well, you know, for hepatitis, they do liver biopsies often. And they stick a needle in your liver. And it just doesn't work out for routine testing to do that kind of thing.

Q. What does it mean to have it reliable?

A. Reliable is if you do it on this blood sample and that number you get, you believe that number, it always comes out to be that number. If you do it again, you're going to get the same sort of number.

Q. And that probably leads us to No. 3, stable.

A. Yeah. This is really crucial, because there is a lot of changes in blood once you take it out of somebody's body. And if the thing you want to measure disappears in the next minute or so, you know, tough luck; you're not going to—that's not going to be a test. So you want it to last definitely for minutes but best is if it will last for hours.

Q. There is a reference here to constant while healthy.

A. Again, you want—if I measure this thing in a person today, I want to get almost the same number that I got yesterday, if the person is still in the same state of health. And next week, I should get the same number. It should be a very small range of the values that I'm going to get.

* * * *

[Pages 202, line 22 through Page 203, line 14]

THE COURT: Be seated, please.

Members of the jury, I read to you yesterday what an expert or opinion witness is. It's a person who has specialized knowledge by scientific, technical, specialized training that will assist the trier of fact, the jury, to understand the evidence. And that type of witness, an expert or opinion witness may testify in the form of an opinion.

The Court will accept Dr. Stabler has an expert or opinion witness in the areas of hematology, oncology, internal medicine, metabolic medicine as to B12 and folate,

and the area of the state of prior art at the relevant time of this patent. Those areas of expertise.

Is there anything else you want to—

MR. WHITEHAIR: I think we were also talking about what treating physicians do with the tests in her area of expertise.

THE COURT: Well, she may testify to that as long as it falls within one of the fields of expertise.

* * * *

[Page 204, line 1 to Page 209, line 3]

Q. We left off with your testimony late yesterday in the middle of an exhibit. Why don't we return to that exhibit and ask to you turn to the first small book with the white cover, first exhibit. We call it Demo 1 but it has a tab 1. Do you have that in front of you, "desirable traits of a useful diagnostic test"?

A. I do.

Q. We've gone over the first three, and I think we were in the—finishing up with 4 before we jumped on. Why don't we just go back. Talking about "constant while healthy." What do you mean by constant—or relatively constant, I think is the word you use in the exhibit?

A. What I mean is that if you measure something with this test while the patient was healthy, there would be a really tight range of values that you would get. The value from yesterday would be very similar to what you got today or what you get next week.

Q. Well, isn't—I'm sorry if I interrupted. Isn't that a problem with something like a glucose test? Doesn't that vary all day?

A. Well, it can, which is why they usually use fasting glucose, because that's much—you get much tighter numbers if you do it at the same time of the day.

Q. What do you mean by fasting level?

A. Before you eat anything in the morning.

Q. Let's talk about "correlates," the next one. Now, this appears to be a little more formal definition than the other ones you described. Is that because I asked to you use the judge's clarification or interpretation of the patent word "correlates"?

A. Correct.

Q. Let's translate that into the way in which you use these terms and phrases in your search for a desirable or a useful diagnostic test. What do you mean by "correlates"?

MR. HIGGINS: Objection, your Honor. He said that it related to your interpretation of correlate, but I don't believe it has the complete definition of "correlation" as your Honor expressed in the Court's order.

THE COURT: We'll go into that later. The objection is overruled. She may answer.

BY MR. WHITEHAIR:

Q. Let's just talk about how it works for you in your day-to-day work.

A. Well, what I say there is the marker correlates mutual or reciprocal relationship with the disease state compared with the healthy state. And to use an example, like we were using the diabetes example, there, a mutual relationship would be that the elevated blood sugar or blood glucose correlates there with the diagnosis of diabetes. You if you have diabetes. The reciprocal would be if the blood sugar is actually normal, then you don't have diabetes.

Q. How—how does a doctor decide if something is elevated, when you talk about this term "elevated"?

A. Well, that's addressed somewhat in No. 6.

Q. Okay.

A. Because—for each person, see, has their own value, which—while they're healthy. So that they would stay, like I

said, in the tight values. They would stay at that same number. It wouldn't vary very much. But when they get the disease state, it will be elevated for them.

A lot of times you don't have the luxury of having previous tests, and then you're stuck with comparing the person against some kind of a reference range. There is lots of names for those, and that's determined by looking at the numbers that you get from a big group of people who you think are all normal; and, you know, we call that reference range, normal range, population range. There is just a whole bunch of terms.

Q. Let's turn to this measurable difference from healthy. What are you capturing here?

A. Well, this is the ideal test, is that you have all of the normal values for a person. Like I said, if you kept doing maybe yearly a test, like they do for glucose for people that it's staying at a certain nice, low level; but if the person then develops diabetes, there is now such a big jump in the number that there is no question that there is a difference between the normal state and the disease state. And it's great when you have individual persons.

But what we do when you don't have serial levels like that is that again we have to study a disease population, so you would study a group of people who all have diabetes, like for the glucose, and compare the numbers you get there, that range, against the numbers you got in a group of people who were normal. And what you are really hoping when you design these tests is that this is a really big difference, there is no overlaps, and that it will be easy to see whether the value is in the diseased vs. in the normal.

Q. What do you mean by "treatment available"?

A. That's medical bias here, is that, you know, we're doctors and we want to be able to fix things, so is it good to know something bad, like a high blood sugar? If there is no treatment, most patients don't really want to know bad news that doesn't have a treatment. And most doctors don't want

to know that, and it's actually hard to get tests paid for that don't—that don't lead to you doing something, some constructive action.

Q. "Predicts outcome."

A. That's the same sort of medical bias, where the answer really has to mean something. It says—it directs you that—to say that, Oh, I know, I found this high level, like if, say, the child is so bad with diabetes that they're in a coma, you find this really high glucose level. Say a high level, a really high level, would be 800. You find that and you say, Oh, boy, as soon as I give insulin, this patient will wake up. And you know that that high level predicts what will happen. And so those are the kinds of tests that you want.

Q. "Early warning system"?

A. And again, that's a big medical bias—is that if you're already so ill, so impaired by the time the test is positive, then people aren't that enthusiastic about being tested for it. The best tests show you early on in the course of a disease in preclinical states like we talked about yesterday that something is going wrong. And then if it's a good test that has treatment available, then you're going to do something about it before it's too late.

Q. I take it a diagnostic test is useless, then, if it comes back normal or unelevated.

A. No. No. That's what we do. We do tests in order to figure out which of the things that we suspect are true. When a patient comes to see a doctor, they don't say, Give me this test, usually. They say, I have these symptoms. And while you're talking to them, examining them, you get the differential diagnosis. That's the term of you think what's the most likely cause, No. 1, No. 2, No. 3. And then all our tests are directed to saying, Well, how I will exclude each of these, so that if the test comes back negative, you just cross it off. Okay. And then you start dealing with the other things that are still on the list. And that's how we arrive at a final diagnosis. That's how we do it.

* * * *

[Page 226, lines 21-23]

MR. WHITEHAIR: Pardon me, your Honor. I believe—It's in our laps. Let's look at it here, specifically Demo Exhibit 2 in the small book.

* * * *

[Page 228, line 3 to Page 230, line 6]

THE WITNESS: So I want you to focus here on this line, because this is the central part of the whole pathway. And homocysteine is—these are all amino acids, which is the name of the kind of little compound they are. And homocysteine can get converted to methionine by that enzyme. And this is where you need the folate and the vitamin B12. When that happens, you use methionine for itself. You need it. But also, it gets activated. This is another enzyme. Once it's activated, it participates in hundreds of reactions. It's very crucial that you have that. After it does those reactions, it's converted to something else, something else, and converted down to homocysteine again. So now we have a circle. We've actually recycled that homocysteine. But homocysteine is at a branch point, so it could go one way, or it could go this way. When it goes this way, it goes through a couple reactions. It turns into cysteine, which is another one of the amino acids that you need, and that can be broken down. And you just—what you don't need just comes out in your urine. This is really sort of one way, that way; and this is a circle.

BY MR. WHITEHAIR:

Q. Thank you. Did you also prepare an illustration that helps us understand the different states of the body that might be processing this pathway?

A. That's correct, because people have been studying which way it's going to go—it's called the regulation—for decades.

Q. Let me have you then take up Exhibit 3A, and in the jury books it's Exhibit 3. They don't have the A on any of the original demonstrative exhibits. That's just for the blowups. Go ahead and tell us what you're trying to show here, Doctor.

A. Now, you also need methionine. You eat methionine. It's in your food. But what about when you're not eating, overnight, or fasting? You still have to have this crucial activated methionine. So when this has been studied, it turns out that the methionine—I've abbreviated it "meth," and the homocysteine—this is a standard abbreviation, H-C-Y-S—just circles around a number of times before it goes down the branch point. That's how you conserve your methionine. Now, say you eat methionine. And there is a lot of methionine in high protein foods, so I'm using as an example steak dinner, where you will get a whole lot of methionine. So here you'll activate it, you'll run the reactions you need until you're down to homocysteine again; but at this point, see, the body is really in balance. It's regulated and something tells it I've got plenty of methionine, let's get rid of it. And it will go through all these reactions to cysteine, and all the extra goes out in your urine. And this is happening all the time, every day, back and forth to keep it all in balance.

* * * *

[Page 232, line 17 to Page 233, line 9]

Q. Let's turn on Exhibit 4 and ask you if that's the chart that you prepared.

A. I did.

Q. That shows at least of these three topics; that there is checkmarks in the methionine list; right?

A. Correct.

Q. And one is cysteine?

A. Correct.

Q. And this indicates that lack of a known role of homocysteine?

A. That's right.

Q. Given all this, was your lab looking for a diagnostic marker to determine vitamin deficiency?

A. To just use as a test, no. But yes, like I said, we want to understand the pathways. You know, it's more global than just have a test. We want to know what's going on when you perturb these pathways.

* * * *

[Page 234, line 21 to Page 235, line 6]

Q. What was your working theory on what would be subnormal or what would be happening in your measurement tests on this pathway?

A. Well, we had to go with what people had been speculating, which would be that methionine would be low because that's what the prevailing theories were; that that was very important.

Q. Was there actually a study out that you were relying on for that?

A. Yeah. We did read a study from a Dr. Parry which—

Q. P-A-R-R-Y?

A. Right.

* * * *

[Page 235, line 19 to Page 236, line 7]

Q. Just take a quick look at that, just to confirm that this is the study you relied upon.

A. So No. 35, the title of it is "Serum Valine in Methionine Levels in Pernicious Anemia under Treatment," by T.E. Parry. I can read the first part of a paper—like this has a summary, usually, or an abstract. So if you read in that first part a sentence sort of near the bottom says, "The serum

methionine level is subnormal in pernicious anemia in relapse." Relapse means not being treated. "It rises to normal in 48 hours after treatment," so it's low; and then it went to normal after they got their treatment.

Q. All right. Now, then they reference that methionine levels actually correct with B12 and folate?

A. That was the gist of this paper.

* * * *

[Page 236, line 13 to Page 239, line 19]

Q. * * * Did you put together a list of the possible metabolic changes that you and the lab were considering when you undertook your experiment?

A. I did.

Q. And let's just look at the first of a series in Exhibit 5. And these are just for your lap. We'll call these laptop exhibits. Exhibit No. 5. Why don't you walk us through. It looks like there is two different statements on there. Why don't you just tell us what this is about.

A. At the top, I've written, "Possible Metabolic Changes." And No. 1 is just to remind you what this pathway is; that the homocysteine in purple there. By action of this enzyme in the circle, you see it shows that it needs B12 and folate, is changed to methionine, and that if everything is just right, there would be just a normal level of the amount of methionine, homocysteine, and cysteine that would be present. It would just be what—a baseline level.

Q. What are you showing in No. 2 below?

A. Well, No. 2—now, the red in that block is supposed to say, now, if you're B12 or folate deficient, then that enzyme will be blocked, see. It doesn't have the partners. It's not going to work as well. So the two things there that we're showing that might result is that methionine would be down because you're not making it and the homocysteine would be high because you've blocked changing it from

homocysteine to homocysteine to methionine. But cysteine would be just the way it is, normal.

Q. Did you try to consider any other possible changes?

A. We did.

Q. Let's turn to the next exhibit and explain the number 3 that you added.

A. I've repeated No. 1 and 2 here on the page so you can look at it simultaneously. But No. 3, you have this block, so the homocysteine is not going to be—to the methionine. But what if that branch point gets more active? The enzymes that carry homocysteine away by changing it to cysteine, they could get a lot more active. They could pick up the slack, in which case methionine would still be low but now cysteine would be high because you're making more cysteine. And then—but the homocysteine is now going to be normal because the—those other processes that make cysteine have taken it away.

Q. Okay. So is that pretty much all the options that you have in this kind of a pathway?

A. No.

Q. Go on. Let's—we're going to go to No. 4—No. 7, but we have this in blowup so you can perhaps make some more illustrative comments, so we don't we have us take a month to reset our thing. This is Demo Exhibit 7A for the record. And Dr. Stabler, if you'd just confirm for us that this is simply a blowup of what you were just looking at as Exhibit 7.

A. Correct.

Q. Why don't you go ahead and tell us. You've picked us another path.

A. These are the ones that we've already talked about, the possibilities; but I over simplified. It turns out there is another enzyme that can do this reaction, homocysteine to methionine. And this enzyme doesn't need B12 or folate. It

uses this stuff called betaine instead to do it. So people had speculated—and it's totally possible—that this enzyme, which would just kick in when this was blocked, the B12 and folate dependent one—when that was blocked, instead this enzyme would pick up the slack. If that happened, you wouldn't expect any changes. Homocysteine, methionine, homocysteine, cysteine, they're all just going to be the same.

Q. Recapping your exhibit, what tends to be the most likely outcome if you look at these choices? What was your working hypothetical?

A. Sorry.

Q. What was your working hypothesis going in?

A. I bet that methionine would be low. I mean I had to believe what other people were saying and had been writing about it for years, so I thought methionine would be low. Of course, we hoped there would be other changes. We wanted as many as possible. We hoped that homocysteine would be high.

Q. How about cysteine?

A. Same thing. There really wasn't that much known about cysteine changes, so that I reserved judgment. Didn't know.

* * * *

[Page 247, line 14 to Page 248, line 1]

Q. Think back to your Exhibit 7, which showed all the possible metabolic changes you recall with the black circles and the three red circles. The bottom one had the betaine pathway. You were basically balancing out which of these things was the most likely of those four pathways, the stable state, the second third and fourth. Which one did you find now with this lab discovery?

A. We didn't find any of them, because the only abnormality we found was that total homocysteine was elevated. And we didn't find that methionine was changed.

Q. Was this a bad result for you?

A. No. It posed problems in having to try to explain to other scientists why methionine was not low. * * *

* * * *

[Page 248, line 4 to Page 252, line 18]

Q. You made some comment about this earlier. Was homocysteine going to be an easy marker to try to track and manage in this process?

A. No. Because of its chemical structure, it means that it's actually hard to handle in the lab.

Q. Let's set this down, have you go back in. And we're going to turn to a couple of charts about these sulfur bonds just so we understand why it's complex. We don't need—I think this section is not designed to teach everybody all about biochemistry but just to understand this complication. Let me have you turn to Exhibit 33 in the big book. And we're going to use 34 in a minute. And really, all I want you to do is just look at these red Ss. The rest of the chart, we could come back to some other day. But right now, I just want to know if these red Ss are going to help you explain why the total homocysteine test was a challenging test to undertake and to use.

A. That's right. If you look on this chart, you see that we've listed the—under the word compound, we list homocysteine and cysteine and albumin. And each one has an S there. That's a sulfur. When you combine it with an H like that, it's a sulfhydril. And the problem with these sulfhydrils is they don't like to be by themselves. They're always wanting to combine with another sulfhydril or something else.

Q. Albumin: What is that?

A. Albumin is a protein that thickens your blood. The reason plasma is thick is because it has a lot of this albumin dissolved in it.

Q. And it's got a bunch of sulfur on it?

A. And it has all these sulfhydril groups, these SHs.

Q. And what's Exhibit 34 designed to illustrate?

A. It's to show you the way homocysteine is actually traveling in blood, because it's not staying by itself. There is incredibly small quantities of just the homocysteine with that SH group that you saw on the previous page. Instead, what you have is listed here on this left side is a compound. The top one is two homocysteines find each other, and their sulfhydrils bind together. Now you see that they make this sulfhydril link or bridge, SS. See the red? And that's two of them together. And that's what we call homocystine. It's a disulfide, two sulfide, disulfides, of homocysteine. Then you have two of them. And there is hardly any of that. Look over to where we say the percent of total—and by total there, I mean total homocysteine.

Q. Not total of everything in the serum?

A. No. Total of how much homocysteine that there would be, all the kinds; and it's really low. It's under 1 percent, and then you can get an actual concentration. See, we use this slide for when we give the talks to the doctors. That's why I put the concentrations there. Okay. Then under it is one that shows that the homocysteine often makes a disulfide with cysteine. That was the other thing we measured. That's called homocysteine cysteine disulfide, and you could see the two Ss there.

Q. Can we just call that MDS from now on?

A. You could.

Q. Okay.

A. And there is more of that. There is about 30 percent. Here we got 28.4 percent. So there is more of that than homocystine. Then the rest appears mainly to be bound to those groups on albumin onto that protein because it has these sulfhydrils sticking out and it sort of just sops up

homocysteine. Am that's actually the bulk of it. And here I have it as 71 percent. Now, these things aren't static. They appear to be changing. They're changing partners in your blood while you're living, and then they also change once you take the blood out of somebody.

Q. Why don't you measure one of these three? Do you need to measure them all? What's the story there?

A. Well, what had been determined was that their changes are so marked after you take the blood out of somebody that things disappear. It looks like the things that are the homocystine or the mixed disulfide sort of disappear in time from that blood sample, especially if you start freezing and thawing it, and it all ends up on the protein. And that's what caused all these problems in saying what is a normal concentration of homocystine, plus look how little there is of homocystine.

Q. So when you try to measure it, then, in your labs, were you trying to catch every single one of these?

A. That's the whole concept of a total homocysteine, is that you can sort of standardize the situation by releasing it from protein, releasing it from those bonds, and let's get it all. And then it won't matter if—how long we leave that blood sitting on the bench, how many times it was frozen. All these little things that could have a huge impact on it don't matter if you decide I'm going to measure it all.

Q. Is that why the patented discussion typically talks about total homocysteine?

A. What we did was total homocysteine. That's right. That's what we do.

Q. Let's put some chemistry behind us for a while. You talked about these scattergrams. You found this homocysteine jumping out several stories high. Was this just corroborating or showing what had already been done in the literature before?

A. Nobody had measured total homocysteine in a patient with B12 or folate deficiency.

Q. So did you go ahead and publish this information?

A. That's right. We again submitted an abstract to the same meeting. But now it was 1985, and I presented it in December in '85. It was published in the abstract book.

Q. And let's just turn, just to hold our spot—Exhibit 40 is the abstract of the '85 conference you attended?

A. Yes.

Q. How did this presentation go this year?

A. Oh, maybe there was a little bit more interest but not much. Again, you see the doctors who were doing vitamin B12 research and then the general doctors who attend this meeting also just to learn and keep up—they really were satisfied with vitamin B12 levels and with folate levels as, you know, the diagnostic be-all. That's what it was. And so again: All right, but why do you want a new test?

* * * *

[Page 252, line 25 to Page 253, line 17]

Q. And just for the record, you published this in the Journal of Clinical Investigation, Exhibit 41?

A. That's correct.

Q. All right. So I take it that since there was really no response to you, the logical next step was to give up on this direction. This test wasn't going anywhere. What did you do next?

A. That wasn't quite how we thought. We thought that the test was so good in Dr. Lindenbaum's gold standard patients and was even—you saw that those infrequently treated patients were often abnormal before they had any other symptoms, so we thought now we have tools to tell whether the patients who have much less classic abnormalities due to B12 deficiency or folate deficiency, or their

vitamin levels are only a little bit low or actually normal, below normal, or there were just a host of questions that could then be answered by using these tests, total homocysteine, methylmalonic acid, to show a deficient state.

* * * *

[Page 255, lines 6-20]

Q. What did you think you had that deserved a patent?

A. The first time that anyone showed that the total homocysteine correlated with B12 or folate deficiency, and that the study, like the study—Dr. Lindenbaum's neurologic—that was in the New England Journal of Medicine. That's the best medical journal—showed that it was useful in patients who had atypical problems and that would be missed by your standard diagnostic methods that were in use then.

Q. Was there also a specific proposed method for measuring total homocysteine in serum?

A. And that's right. We also—our method was different than the couple of other methods that had been described. And ours was very good because of using an internal standard so that we could take care of those problems of all those sulfhydrils getting together while you were preparing the blood.

* * * *

[Page 280, line 5 to Page 281, line 9]

Q. All right. So our elevated numbers comes back. And what does—let's just take in the total homocysteine case. You've ordered the single total homocysteine test, it comes back elevated. We'll just pick a high number so that it's not a big fight here. What does the doctor then do next?

A. The doctor will prescribe vitamin therapy.

Q. And what therapy will the doctor describe—prescribe?

A. Completely depends on that patient's story, their history, what vitamins were they already taking. Very common that someone comes in who is already taking a multivitamin. If they have a high total homocysteine, you're going to give them vitamin B12. You know they're already getting folate, so the doctor is going to individualize.

Q. What it—what if the patient has no history of taking any supplementation?

A. I think now that most doctors are giving both, both folic acid and vitamin B12, because there is so much in the medical literature in the last couple years about the benefits. Even though they haven't yet been ironclad proven, there is so much out there saying that people will benefit if they have their total homocysteines lowered. And the best way to do it is to give them both folic acid and vitamin B12.

Q. Are you talking about giving these people shots for the rest of their lives?

A. Well, I think the reason it's been popularized is because we have figured out that you can use high-dose pills of vitamin B12.

Q. Actually you can take it in your mouth?

A. You can take it—even the worst-case patients of pernicious anemia can be treated with vitamin B12 pills.

* * * *

[Page 303, line 3 to Page 305, line 18]

MR. WHITEHAIR: Would you mind, Mr. Zuckerman, so I make sure it's accurate, because it's a little bit different than the notes that I wrote.

THE REPORTER: "Let's switch gears a little. The defendant in this case, LabCorp, has suggested that the total homocysteine only test is widely used for a broad array of things other than to determine a patient's vitamin deficiency levels. What's your reaction to that?"

THE WITNESS: I don't agree with it. I think that there are many CONDITIONs that are associated both with having the B12 or folate deficiency and an elevated total homocysteine.

BY MR. WHITEHAIR:

Q. Well, I understand there is a number of conditions that appear to be associated with elevated total homocysteine. What do you say to that?

A. I SAY that the underlying thread, the thing that links them, is that they're associated with either B12 or with folate deficiency.

Q. Did you take some time to put together a chart based on your own assessment of the different mechanisms that lead back to this vitamin connection?

A. I did.

Q. The jury doesn't have it, and I want you to describe it. Under our rules, it needs to be discussed before it can be put in front of them, or it may not be able to put in front of them; so if you would just work with me through what we call a foundation of an exhibit. You have a copy of what's been marked for identification as Exhibit 8 in front of you.

A. Yes.

Q. Tell me what—what were you trying to accomplish in this exhibit?

A. I was trying to explain the cause for having a vitamin deficiency. THERE S really three mechanisms where you get to have a vitamin deficiency and how that related to each of the conditions that has been seen in—with elevated total homocysteine, also.

Q. Let's talk about the mechanisms, and then we'll talk about the conditions. What are the mechanisms that you see in this vitamin deficiency scenario?

A. Having a poor diet is the most common cause probably of folate deficiency, because it's found mostly in fruits and vegetables or organ meats, and a lot of people don't eat

those, so that diet has always been incredibly important as a cause.

Q. What else?

A. Then you—you can have problems absorbing vitamins. There is known abnormalities of the stomach and the intestines which cause you not to take in the vitamin, even though you're eating plenty of it in your food.

Q. Are there any other mechanisms?

A. And then there are substances that you it can ingest or conditions you can have where the vitamin does not work optimally, and we call it sort of a vitamin defect, in that the enzyme is inhibited or the vitamin is in the wrong form, or a lot of different problems like that.

Q. Now, for each—were there any other substantial mechanisms you could think of?

A. Those are the main—I would say those are the main ones.

Q. Now, you laid those against each of the conditions that have been suggested as associated with elevated total homocysteines. Is that right?

A. Uh-huh.

Q. And you laid them out here and checked off the condition and each of the mechanisms that was implicated?

A. Correct.

* * * *

[Page 309, line 23 to Page 312, line 21]

Q. I want you to take a moment, Doctor. I want you to look at all seven of these. And I want you to tell me whether in your opinion these are conditions that are diagnosed by a total homocysteine test.

A. No.

Q. The doctor doesn't take the test to see how old their patient is?

A. No.

Q. What sex they are?

A. No.

Q. Whether they've been smoking?

A. No.

Q. Whether they've been drinking?

A. No.

Q. Does the doctor know what the medications are?

A. That's parts of the history—

Q. Will the doctor—

A. —to know, yes.

Q. What about this kidney disease?

A. Well, there are special tests for kidney disease.

Q. This is not a test—

A. Creatinine, BUN, yeah. You don't get this test.

Q. Is it among the tests you might use?

A. No.

Q. How about for thyroid disease?

A. No, not at all.

Q. Let me ask you to turn to the next chart. Did you compare—did you put together a list of what was—when the total homocysteine test was useful?

A. Yes.

Q. And let's turn to Exhibit 9. And going down each of these, I think you're just reiterating what you said. 1 through 7 are all nos, and then you've got two—we were sly. They're green. Tell me what 8 and 9 mean.

A. You use the total homocysteine to detect B12 deficiency and folate deficiency and/or both.

Q. All right. Now, did you also compile a list of the select manifestations, the various things that are caused by B12 and/or folate deficiency?

A. I did.

Q. And where will we find that?

A. That is the No. 10 demonstration.

Q. Well, not to belabor it, but I—you've been talking for most of the day about a variety of conditions that get called out in anemia. You talked about some tingling hands. Is this an attempt to try to capture most of those?

A. These would be the manifestations that a person could have if they were B12 or folate deficient.

Q. And that's what's under the—

A. That's on all — all of these different things is what is seen in various patients who have the deficiency.

Q. And then the recommended treatment?

A. You treat the deficiency.

Q. You've listed neural tube defects near the bottom. What are those again?

A. Those commonly called spina bifida. People may have heard that word, and it's problems that happen in the spinal cord in the nervous system really early in pregnancy. And it's clearly related to whether the mother has enough folate in her body and is getting enough daily, very early in her pregnancy, when she gets pregnant.

Q. You listed heart attacks here.

A. Well, that's what all this vascular disease association shows. If you can actually measure serum folate in a group of people like they did for the nurses health study and those—well, there they looked at the intake. But in a Cana-

dian study, they actually measured the serum folate. And the people of the low serum folate or the people who don't eat the folate, they have higher risk of having heart attacks. That's why everyone is so excited, because there is something we can do about it.

Q. And the same issue for strokes?

A. And the same thing is true in strokes. They show that in the NHANES study.

* * * *

[Page 322, line 19 to Page 323, line 14]

Q. Let me ask you this question: What if a company in the business of selling assays for total homocysteine made the following statement to the doctors ordering the tests: This test is intended to be used as an independent risk factor for vascular disease and is not intended for the diagnosis of folate or vitamin B12 deficiency. Do you consider that good medical practice?

A. I do not.

Q. What's wrong?

A. Well, if I ordered that test on a specific patient, the test comes back, it's high, what do I do then? I say, oh, this test—this total homocysteine doesn't show that you're vitamin deficient because it's the way this test is used. So I don't offer therapy? I just let it be? I let it be high, instead of treating with the combination, or one or the other, depending on everything else I know about the patient, and say I'm sorry, bad news, you have a risk factor?

Q. What's your medical opinion about a doctor who would fail to treat in response to that high homocysteine level?

A. I think right now people would think, and I would agree, that that's actually malpractice.

* * * *

[Page 324, lines 13-25]

Q. Let's turn to Exhibit 66 in the big book. And tell us what this article is from and what it tries to teach.

A. This is from the JAMA, Journal of the American Medical Association, that comes out weekly. It's very widely read. And it's August of this year, 2001. See that there at the bottom? And it was written—you could see there is a big list of authors, and it includes people from University of Colorado—excuse me—University of California and then people from the big nutrition center in Tufts that's very highly regarded, as well as people from the Harvard School of Public Health and an international expert even from the Netherlands, plus other authors; so it's a big, collaborative effort of a lot of different authors.

* * * *

[Page 327, line 13 to Page 328, line 19]

Q. Just the conclusion. Those four lines.

A. "In the meantime, since combined therapy with folic acid and cyano-cobalamin is well-tolerated, it is reasonable to consider routine therapy in men older than 45 years and women older than 55 years."

Q. And on the front page—were you reading from the back?

A. Yes.

Q. I'm sorry. If you would read the conclusion section on the front page, starting, "Folic acid," and then when you go through it tell us what CHD means.

A. Okay. This is in the abstract in the front page.

"Conclusions: Folic acid and cyanocobalamin supplementation may be cost-effective among many population subgroups and could have a major epidemiologic benefit for primary and secondary prevention of CHD," coronary heart disease, "if ongoing clinical trials confirm that homocysteine lowering therapy decreases CHD event rates."

Q. Thank you for that. And what are these homocysteine lowering therapies?

A. They are combinations of vitamin B12 and folic acid. That's what they refer to in this study, but it could also be vitamin therapy, one or the other.

Q. What's your opinion of the relationship between total homocysteine and vitamin B12 and folate status in a human being?

A. I think they're intimately linked.

Q. You're crossing your fingers?

A. Yeah. They go together like this.

Q. Other than to determine vitamin deficiency, is there any other substantial use you know of for ordering a total homocysteine test?

A. No.

* * * *

Dr. Sally Stabler—Cross

[Page 458, line 24 to Page 459, line 3]

Q. But that's not something you or Dr. Allen discovered, is it?

A. Renal disease? No, we discovered that vitamin B12 and folate deficiency correlates with an elevated total homocysteine.

* * * *

[Page 492, line 5 to Page 494, line 4]

BY MR. HIGGINS:

Q. Dr. Stabler, I'll read from the order here on the word "correlating" of Claim 13. It says that correlating—"The term 'correlating' in Claim 13 is a verb that is construed to mean 'to establish a mutual or reciprocal relationship between.' Okay. Do you understand that?

A. Okay. Uh-huh.

Q. And it says—it further says, "that describes a discrete step in a sequential process." So my question is once a body fluid is assayed for total homocysteine and the result is elevated, what step is performed that falls within the definition of "correlating" as I've just read it to you?

A. Losing me again here. The mutual relationship is that you see that if the level of total homocysteine is elevated that there is a deficiency of cobalamin or folate.

Q. Well, the definition says to establish a mutual or reciprocal relation, and that describes a discrete step in a sequential process. So what step takes place to establish that an elevated level is—has a mutual or reciprocal relationship with a deficiency of cobalamin or folate?

A. Well, if you had already done the total homocysteine on someone and later you did it again and it was higher, then you would know that the step would be that you would compare the first one to the second one and say it's now higher, so this person now has a deficiency of cobalamin or folate.

Q. So in order to establish this relationship, it requires that a patient's homocysteine be measured twice?

A. That—that would be one use that you did it. That's how you would know for one particular person it might be elevated. But you might not have done it twice. That's one example of how you would do it. Other ways, you would compare it against what you know in the literature to be considered elevated.

Q. So it's your testimony that by obtaining an elevated—an elevated level of total homocysteine that you can look at the literature and determine that that elevated level for a particular patient is the—has a mutual or reciprocal relationship with a deficiency of cobalamin or folate?

A. That's in general how you would do it.

Q. And so does that take place in the mind of the physician?

A. Well, yeah. The physician will be—is the person who is going to be looking at the number, yes.

Q. And so you're saying that it's sufficient to establish a mutual or reciprocal relationship between an elevated level of total homocysteine and a deficiency of cobalamin or folate by looking at medical literature?

A. Wait. Start over with that one again.

Q. I'm just asking –

A. No, I mean "establishing a relationship"? The literature tells us that elevated total homocysteine is a—seen in cobalamin or folate deficiency. I mean there is reams of that.

* * * *

[Page 506, line 18 to Page 507, line 16]

Q. Well, let me ask you this: What is the minimum that is required to establish an elevated level of total homocysteine with a deficiency of cobalamin or folate?

A. The minimum? The minimum what?

Q. What is the minimum act or step that a physician can take to establish that an elevated level of total homocysteine has a mutual or reciprocal relationship with a deficiency of cobalamin or folate?

A. They have to see the level, and then they have to make the correlation that if they—they have to decide against whatever standard it is they're going to be using whether they think it's elevated or whether they think it's normal for this patient. And then if they think it's elevated, they say this shows that there is a deficiency of either one of these. If they say that I've decided that this is normal, then they say I don't see a deficiency of either vitamin B12 or folate.

Q. And is that all that done in the physician's mind?

A. Everything is done in the physician's mind.

Q. So in other words, to fall within the second step of Claim 13, all—all that is required is a mental step?

A. It's—there is no surgery involved or no—I can't—how can I answer that? Everything you do, you read something, it's a mental step. You—I don't know—I don't know what that means.

* * * *

Dr. Sally Stabler—Redirect

[Page 519, line 20 to Page 520, line 3]

Q. To your knowledge—oh, I see. To your knowledge, Dr. Stabler, based on all the things you've discussed since you started here—to your knowledge, did anyone ever suggest measuring total homocysteine in those circumstances?

A. No.

Q. In fact, before the prior art dated November, 1985, had anyone ever correlated an elevated total homocysteine level with a deficiency of vitamin B12 or folate?

A. No.

* * * *

Frank McPike—Direct

[Page 553, lines 15-20]

Q. Was CTI at any point in that time taking the position that homocysteine was a marker for vascular disease?

A. No. It's always been a marker for vitamin deficiency. I guess the good news was that this was another—another disease indication that could utilize the services of this diagnostic text—test.

* * * *

Frank McPike—Cross

[Page 565, lines 17 to 21]

Q. And as a matter of fact, CTI claims that LabCorp performs, when it performs the single homocysteine only test, even utilizing the Abbott method—CTI claims that that activity is covered by claim 13; correct?

A. That's correct. That's correct.

* * * *

[Page 572, lines 20 to 24]

Q. Now – and the statement as contained in this press release dated January 5, 1999, is consistent with your position, which is that every single homocysteine test done in the United States, CTI is entitled to a royalty on?

A. Yes.

* * * *

Frank Ryan—Direct

[Page 610, line 6 to Page 611, line 10]

BY MR. WHITEHAIR:

Q. Do you use the term "diagnose"? Do you know—do you have a view of what that word means?

A. I've—I know what the word means, I think.

Q. Do you know what the word—do you consider that be synonymous with the word "correlate"?

A. No.

Q. How would you distinguish those, Doctor?

A. Well, diagnose. If somebody has prostate cancer and you go and take out the prostate and you identify that they have cancerous cells in their prostate, you've made a diagno-

sis that there is prostate cancer. If a person like the—C-reactive protein is a test that cames out in the last couple years that looks like one of the better monitors for heart disease. And there is a correlation between the level of C-reactive protein and the chance that you'll have a heart attack in five years, I think is what it says. So there is a correlation. There is no diagnosis there. We haven't made a diagnosis. We're just correlating the chance that somebody will have heart disease, so it's not a diagnosis.

Q. Do you know if there is any therapy available in response to C-reactive protein?

A. C-reactive protein, I would say that things that reduce inflammation in your body would lower your C-reactive protein. I think that like aspirin would probably be good for that.

Q. Do you see the word "correlation" meaning something more to do with probabilities and the word diagnosis more to do with facts of finding a disease?

A. Yes. Correlation is much more like probability.

* * * *

Frank Ryan—Redirect

[Page 620, line 14 to Page 621, line 4]

Q. Now, back in '96, when you were doing these tests—this test, you didn't test for folic acid then, did you?

A. No.

Q. Instead, you just ordered the single homocysteine only; right?

A. Yes.

Q. And you found your level was right in the middle of the reference range?

A. Well, pretty close.

Q. So you took folate; right?

A. Yes.

Q. And the homocysteine level came down?

A. Yes.

MR. WHITEHAIR: That's all I have.

* * * *

Robert Allen—Direct

[Page 646, lines 14-25]

THE COURT: I have explained to the jury what an expert or opinion witness is. And at this time, the Court will accept Dr. Allen as an expert witness in the areas of internal medicine, hematology, and the science and medicine of B12, folate, and homocysteine. And I think these broad areas will cover. And then if you have specific questions and there is an issue of whether it falls within the area of his expertise, I'm going to ask the attorneys to come up to the bench again. I'm not—I don't think it's necessary to qualify him in the area of state of the art. If he is knowledgeable in the main areas and is able to testify about the state of the art, he may do so. And if there is a question, the attorneys can come up to the bench.

* * * *

[Page 684, line 23 to Page 685,line 9]

BY MR. WHITEHAIR:

Q. Do you know what was written at the time about assays of this—in this area, in, say, 1985 time frame?

A. I'm familiar with what textbooks taught about the diagnosis of B12 and folate deficiency, the use of various tests that were in existence and what practicing physicians knew about and what tests they utilized to diagnose B12 and folate deficiency.

Q. Have you compiled that information in the slide materials that you said preceded this lawsuit?

A. I have a series of slides that I've prepared long before this lawsuit started that I've used for many years in giving talks about this particular topic.

* * * *

[Page 687, line 7 to Page 695, line 13]

Q. I interrupted the order of your presentation. Would you go back to Exhibit 87 now.

A. I have that one.

Q. Where are these quotes or—I guess they're all quotes. Where are they from?

A. Well, they're from the chapter on megaloblastic anemia, from Harrison's Principles of Internal Medicine. And the next exhibit, Exhibit 88, has the Tenth Edition and the Eleventh Edition of those chapters. On the slide, the quotes are from 87, but the exact identical quotes occur in the '83 edition.

Q. Why don't you go back, then, to 87—pardon me—and go through this for us.

A. It starts by saying they're teaching that the finding of significant macrocytes—this is big red cells. Remember the normal population range is 80 to 100, and they're saying if it's above that, this suggests the presence of megaloblastic anemia—that can be B12 or folate deficiency. If the macrocytosis is marked, the MCV is greater than 110, the patient is much more likely to have a megaloblastic anemia. The second statement: It should be emphasized that occasionally, not very often, but occasionally neurologic disease may occur with a patient with a normal hematocrit. Hematocrit is also a measure of the number of red cells. So it's saying occasionally you can have problems in a patient that is not anemic. In the last statement, it says, "The normal range of vitamin B12 in serum is 200 to 900. Values less than a hundred indicate clinically significant deficiency." In other words, the B12 test is so good that if you're deficient in your

body, your B12 level won't be just below 200 but it's going to be below 100 if this is of any significance.

Q. What's the next step?

A. I think we've already talked about the two chapters. If we go to exhibit there—Exhibit 88. If we go to 89, we see now a leading textbook for the practice of family medicine. This was published in 1984. And the next exhibit, which is Exhibit 90, has that chapter from which these quotes are taken.

Q. How do you pronounce his name?

A. I would pronounce it Rakel.

Q. R-A-K-E-L?

A. That's correct. I might mention that the authors of this chapter are two professors from the University of Utah. The preceding exhibit was written by two authors, a professor from Harvard and a professor from Tufts Medical School in Boston. So here the textbook is teaching that "the diagnosis of pernicious anemia should be suspected in the elderly individual who develops macrocytic—" that's big red cells "—megaloblastic anemia while consuming a normal diet. Oval macrocytes—" I showed you examples of those on the blood smear "—are the characteristic abnormality in the blood, and their presence results in a greatly increased value for the MCV," not just over a hundred but much above that. "The anemia varies in degree, but the blood hemoglobin level is less than 7 or 8." Normal is about 12 to 16 in symptomatic patients. "Finally, in vitamin B12 deficiency, serum vitamin B12 is greatly reduced, less than a hundred, whereas the serum folate is normal."

Q. What's your next exhibit?

A. Well, after we get past the Rakel chapter, we now have quotes from a textbook of hematology in 1987. This is by Dr. Jandl.

Q. That's J-A-N-D-L?

A. That's correct.

Q. And our exhibit number is?

A. Well, for the quotes is 91 and for the textbook chapter from which the quotes are taken, it's 92. Dr. Jandl is also a professor at Harvard Medical School. He starts out: "The MCV is usually over 115 but commonly 130 to 150. The white count—" these are the white cells that fight infection "—ordinarily is between 3,000 and 4,000 cells per microliter." Normal is in the range of 5- to 10,000. "Platelet counts are subnormal in nearly all patients." These are the little cells that help our blood clot. LDH stands for lactic dehydrogenase. That's an enzyme that's present within red blood cells in the bone marrow. In either B12 or folate deficiency, it's released in the blood. So he's teaching that LDH levels average about 15 times normal in megaloblastic anemia. And then, finally, "Concentrations of serum B12 below a hundred indicate vitamin B12 deficiency sufficient to cause megaloblastic anemia." Now, in this chapter, which I didn't put on the slide back in the 80's, there are two other important statements. First deals with the serum folate level. And it states that the serum folate level, the normal range is 6 to 20. Patients with folate deficiency have values below 3. A similar statement is made in Harrison. 6 to 20 is normal. Below [4] in folate deficiency. Dr. Jandl also explains in great detail about methylmalonic acid, how it's a very sensitive indicator of B12 deficiency, known since the 50's, and goes on to say that this test is, quote, "seldom necessary," end quote.

We go past 92, which is the Jandl chapter. We come to the last quotes from a textbook. This is from Cecil, Textbook of Medicine, 1985, by professor Beck, another Harvard professor.

Q. And what's the exhibit number?

A. For the quotes, it is 93; and Dr. Beck's chapter in Cecil is Exhibit 94. "Neurologic symptoms occur later in some but not all patients. Curiously, they can occur in the

absence of megaloblastic anemia." "A decreased serum vitamin B12 level is decisive diagnostic evidence. Clinical signs generally appear when the serum level is below 80 to 100 picograms per milliliter." "Methylmalonic aciduria—" that's increased methylmalonic acid in urine "—is also a sensitive index of vitamin B12 deficiency." "In practice, assay of urinary methylmalonate is rarely necessary." So that the common theme of the textbooks in the mid 80's is that you suspect B12 or folate deficiency when you have just not big red cells but really big red cells. You have a very significant anemia. You will have a low white blood cell count. You'll have a low platelet count. And the critical test, the gold standard, is either the serum B12 or the serum folate. And in patients with clinically significant disease, the values for these tests are not just below the population normal range, they are way below the population normal range.

Q. What's the use of the MMA test?

A. Well, it existed. It had been known since about 1955. It was known to be a sensitive indicator. But as both Dr. Jandl and Dr. Beck said, it was either seldom necessary, rarely used; and I never used the test, and I don't know of anyone at Washington University or at the University of Colorado that used urinary methylmalonic acid to diagnose even a single patient.

Q. Did you have any personal experience with the way in which these standards might have been used?

A. Well, I have no doubt that informed physicians not only read these teachings but they followed them. And I have three personal examples. The first is one of our CU medical students who did a medical rotation at one of the private hospitals in Denver—I think it was Saint Joseph's—who then took a medicine rotation at University Hospital. The question came up whether a patient might be B12-deficient. And he said, Oh, he had learned that when you think about B12 deficiency, you look for the LDH level. This is a test that's—not only is it made in red cells but it's—can be elevated in heart disease and liver disease. Very

common a patient in the hospital will have had the LDH measured regardless of the disease. And he said he had learned that you don't even think about B12 deficiency unless the LDH is at least three or four or five times normal. The second example: One of the general internists at University Hospital considered by many to be the finest general internist. Most of the faculty went to see him. In the mid 80's, I discussed with him—he realized how important B12 deficiency was. He looked for it. And when he found a patient that he suspected of being deficient and the B12 level came back, let's say 150, clearly below 200 but not below 100 where clinically significant disease occurs, he wouldn't treat the patient. He would follow, get a B12 every six months; and when the B12 level, if it got below 100, then he would institute treatment. Third example is a hematologist at the VA hospital, who at morning rounds one time when the question of B12 deficiency came up, he stated that he never suspected or worked up a patient for B12 deficiency unless the MCV was over 110. When I challenged him on that, he went into the textbooks. And so those are three personal examples of real physicians following the teachings of the text books at the time.

Q. What was the folate teaching at the time?

A. Well, as I said, the folate teaching was again that the hematologic presentation was the same as B12 deficiency: You look for big red cells, they had to be really big, you needed anemia, and the test that told you whether the patient was deficient or not, the perfect test was the serum folate level, not just low but very low.

Q. In 1985, did your research team have an opinion about these teachings?

A. Well, I would say we were—usually don't read chapters in textbooks about your own specialty. I mean if you're an expert in B12 or folate deficiency, you don't—You spend your time looking up chapters on diseases you're not an expert in. We were certainly, however, suspicious that some of these concepts, at least, were inaccurate; and if you

look back through the textbooks, you won't find any documentation for any of these statements. Hematology textbooks in particular, Dr. Jandl's chapter, will have 3- or 400 references. And if you look for these statements, you either won't see a reference after it; or if you do see a reference and you read it, it doesn't really say. And I think what these doctors were doing is they were—they were expressing their beliefs based on their personal experience. And we were suspicious, particularly Dr. Lindenbaum, who had been collecting cases, as Dr. Stabler said, for 20 years. He was sure that every patient didn't have a B12 below 100. And he pointed out to us that there had never been a good clinical study of B12 deficiency since the early 20's. Once the disease could be cured, no one collected large numbers of patients and described what the clinical spectrum of abnormalities was.

Q: What did your lab do next?

A. Well, we decided we would test the textbooks. And if we turn to Exhibit 95, it poses the question at the top: Are hematology and medical textbooks correct in what they teach us about the clinical spectrum of cobalamin deficiency? And there were two possible approaches: We could do the Lindenbaum approach, collect patients, study them very carefully, or we could use the new metabolic tests that we had. The most powerful way, of course, is for the three of us to get together and do both approaches at the same time. And that's what we did.

* * * *

[Page 725, line 15 to Page 726, line 11]

Q. Were the studies you've been describing in the B12 field the ones you'd just been discussing with us?

A. Yes.

Q. Is there anything similar on the folate side?

A. Yes. If we go to 126, this is a one slide summary of a study we did with Dr. Lindenbaum in patients with folate

deficiency. He had collected 100 consecutive alcoholics that were admitted to the hospital with anemia. And he then sorted out what the cause of the anemia was. Many of them were iron-deficient, but he had 37 that had anemia and had megaloblastic bone marrows. And he ruled out cobalamin deficiency. Therefore it—with other things, including response to therapy, they were clearly folate-deficient. He looked at the serum folate, the gold standard for this deficiency. In his lab, the normal was above 2.1. Only 41 percent of these clearly folate-deficient patients had low values for serum folate, whereas when we looked at the total homocysteine, back there with our very first generation assay, our cutoff was 22; and 34 of the 37 patients, or 92 percent, had elevated values of total homocysteine. So here again, the total homocysteine test was clear superior to the serum folate test.

* * * *

[Page 743, line 5 to Page 746, line 23]

Q. With regard to the second concern of the office action, what was your response back to the Patent Office?

A. Okay. The two articles cited—one was by a Dr. Mudd in 1969, concerned a patient that couldn't put a methyl group on the cobalt to make the active form of methyl B12, and so there was a problem converting homocysteine to methionine. And a form of one of these sub homocysteine—subspecies was present in either the blood or the urine. And that was combined, then, with the paper that talked about methylmalonic acid. And again, our response was here we didn't have to talk about what an imaginary person would think, because we cited, which we supplied when we filed the patent, a review article by Dr. Mudd that was cited, in which Dr. Mudd himself, in 1974, five years after his '69 article, and he knew all about all of these genetic defects. And a couple of the kids had already been described with some form of homocystine in their urine due to B12 deficiency. And he wrote and said that he didn't know if this occurrence in these real [sick] kids—whether some form of

homocystine, the two homocysteines together—whether that occurred commonly in these rare diseases, or whether it was a rare occurrence, and that he had no idea whether it ever occurred in adults with pernicious anemia.

Q. Are you describing what you provided as an attachment to the response to office action?

A. Well, I don't think we attached anything. What we did was we wrote what—why we thought the examiners were wrong. We had two of them at that point. This Mudd quote came out of a review article that we had cited in our original specification. So the examiner was already—had that and knew about that article.

Q. And you're referring now to the list of references cited in Exhibit A, on the first and second pages of that Exhibit A?

A. Yes, I am. The article in question is on the second page. And if we go down the column, we start with Malloy, and we get down to the second—second Mudd article, the one that says, "Heritable Disorders of Amino Acid Metabolism, Pattern of Clinical Expression and Genetic Variation," 1974.

Q. What was the next concern proposed by the Patent Office?

A. Well, the second office action—and it also allowed a number of the claims where we were using total homocysteine and MMA. Those were allowed. But there was still a problem—it was primarily with Claim 13 and the wording of Claim 13, whether we were trying to claim any use of total homocysteine or whether it was—it should be limited, which we thought we'd done the first time—whether it should be limited to detecting B12 and folate deficiency.

Q. Dr. Allen, would it be helpful to your testimony at this time if you could see the exhibit that had been put up by the defense that described the first form that you put in the specification and the second form in the amended claim?

A. Yes, it would.

MR. WHITEHAIR: Could I ask as a courtesy, Ms. Harris, if you could put up Exhibit MB. I believe that's the correct one.

BY MR. WHITEHAIR:

Q. You may have MB in front of you in an exhibit book, if that would be easier than seeing it.

A. I have it on my screen. I can—I can see it.

Q. All right. Okay. And what was it that the Patent Office had concern about?

A. Well, the claim as originally filed started out with a method for detecting a deficiency of cobalamin or folate in warm-blooded animals by assaying body fluids for the presence elevated levels of total homocysteine.

Now, I thought that since the first part of that claim said it was a method for detecting cobalamin or folate deficiency, we were clearly limiting our claim to just such uses.

Now, it's my understanding that sometimes when you start a claim that way, it really is a limitation. Other times—and in this case—the Patent Office said, Well, they weren't sure that was a limitation. I think they said it was an intended use. So what they said was, you know, you can only—your claim can only cover a method for detecting deficiency of cobalamin or folate. That's what we meant originally. We were never trying to claim any conceivable use of a total homocysteine assay. So the examiner helped us. The examiner said, Here is how to be absolutely certain—okay—that you—the examiner let us copy the first introduction. There is a little change. It looks like we put in the word "comprising the steps of," and then it says, "assaying a body fluid for an elevated level of total homocysteine," and then a discrete step, "correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate." And our response—I think we did—I think

it's word for word what the examiner suggested. If not, there is some little minor thing; but we agreed with the examiner, and so we amended Claim 13.

Q. And what did the United States Patent and Trademark Office do after—in response to that amendment?

A. They then allowed all the rest of the claims, including Claim 13.

* * * *

[Page 768, line 20 to Page, 769, line 8]

A. * * *. There was a rather lengthy telephone conversation, where we went through the entire what turned out to be a license agreement between Metabolite and Roche Biomedical—or actually with Hoffmann La-Roche. It covered a number of different items.

Q. Did you end up having a conversation about what you would charge if you kept doing tests in the transition period?

A. The first item—and this is a phone call that Mr. Knesel and Dr. Bookout were on the other end and I was on my end. And we sort of took things in order. The first question was if they signed a long-term agreement, would Metabolite give them a price break.

And I responded that I would be willing to lower my charge * * *.

* * * *

[Page 769, line 23 to Page, 770, line 20]

[A.] So once the agreement was signed, Metabolite would charge Roche 43 percent of whatever Roche charged their customers.

Q. Now—and that's for which kind of tests? Are they being done at Metabolite, or are they being done at Roche?

A. These are tests that would be done at Metabolite.

Q. Was there any conversation about what would happen once Roche was able to do these themselves in house?

A. Well, they were very interested in having the rights to use our automated system. And so they asked me what the charge would be by Metabolite if I turned over all of our software, all of our know-how, assisted them in setting up the assays, and also provided any kind of long-term advice or support that they needed.

And I told them that in return for that, Metabolite would like to have a second 6 percent that would go to Metabolite, would not be passed onto University Patents.

Q. And what was the response to that?

A. They thought that was just fine.

Q. Did you start working out the details?

A. Well, the last thing that came up was the issue of what if they used this robotic system for tests other than the Metabolite assays.

* * * *

[Page 771, line 15 to Page 772, line 12]

[A.] And at one point in the conversation, then, Mr. Knesel said to me—he said Dr. Allen, How much would we have to pay Metabolite when we do the metabolite tests if we can use your robotic system for any other system and we don't have to pay you a penny or even tell you about using the robotic system for any other tests?

And I said that I had never thought about it but it would certainly have to be considerably more than the 6 percent.

And Mr. Knesel then said to me, When you do the test for us, we're paying you 43 percent. How about if we do the metabolite test in house, we pay you half that, 21-and-a-half percent? And then they could use the robotic system for any other test, not pay me or not tell me anything about it.

And I thought—

Q. Let me ask: What did you do in response to that?

A. Well, I thought about it for a minute. I thought that this robotic systemic could be used for many, many different tests. I might be giving up quite a bit by agreeing to that. On the other hand, I really felt these metabolite tests were important and that their usage was going to increase markedly and I realized what a nightmare it would be to try to keep track of the others. And so I said that would be fine.

* * * *

[Page 843, line 5 to Page 849, line 21]

Q. Let me go, then, and ask you what is Exhibit 143.

A. 143 is a letter from me with certain attachments to Dr. Peter Wentz, Roche Biomedical dated June 4, 1992.

Q. And that's signed by you on the second page?

A. Yes, it is.

Q. What was—let's just refer to the first paragraph. What was—what were you trying to say there?

A. Well, just talking about our conversation and just telling him that I was glad things were running smoothly. And the second sentence is "I will always be glad to answer any technical questions that arise concerning the metabolite assays and that Dr. Stabler and myself will be glad to answer any questions that doctors might have regarding results or interpretations of the metabolite assays."

Q. Okay. Dropping down to the third paragraph, what are you describing there?

A. Oh, I'm sending him some tables and some literature reference that—I think he mentioned they were interested in coming up with a, oh—a physician education brochure. They were always from the beginning either through brochures or messages on test reports teaching patients [sic] how

to use the total homocysteine and the other metabolites to diagnose B12 and folate deficiency.

Q. With regard to the other attachments, what did you understand was the use to be made of your attachments by LabCorp—or, I'm sorry, Roche at that time?

A. They could use them or the information considered in them to prepare this physician education piece.

Q. And did that include changes on your patient report protocol?

A. There wasn't any patient protocol here, but they—as I testified earlier, they—I mean I suppose—well, they did not have permission to make any significant changes. Again, that was our report. I assume that when they started doing the tests themselves, they would have their own report.

Q. Did you write paragraph 2?

A. Yes, I did.

Q. What were you explaining to Dr. Wentz in paragraph 2?

A. Well, I could read the first couple of sentences. It says, "One aspect of the metabolite assays that I did not mention in our conversations concerns the occasional request that only one of the metabolites be performed rather than all four. I have always refused to do this because I do not believe that it is good medical practice." And then I go on to explain how I'm afraid that if at this point in time, dating back to 1988, that if you just gave many physicians just one metabolite—for example, the homocysteine—they might not understand what to do with that result. If you'll recall, in the middle and late 80's, there was really no place for a doctor to go and read about information about these tests. This didn't enter the textbooks, oh—my chapter was published sometime in late '92. The other textbooks didn't pick up on the MMA and homocysteine assays and how they should be used until the mid 90's. And as you'll also remember when Mr. Higgins was cross-examining Dr. Stabler, there was articles

published in the vascular disease literature talking about how folic acid would lower anybody's homocysteine. And I was literally terrified in these early years, not now, but in the early years, that if we just provided a total homocysteine value and the result was elevated that a doctor might just say, Oh, oh, okay. I'll just treat with folic acid. And as you heard Dr. Stabler testify, that can be incredibly dangerous if the patient is B12-deficient, because the folic acid can actually correct all of the hematologic problems, the doctor then thinks, "I made the right treatment choice," but it doesn't do anything for the neuropsychiatric problems. They can develop anew or they can progress. So I felt it was important at this point in time and earlier to make sure the doctor couldn't make a mistake. Same price, they got the total homocysteine and they got a methylmalonic acid. And so right in the interpretive report, you didn't have to suggest that he get it. It was staring the doctor in the face. And then if that MMA was elevated, the doctor would say, Oh, okay, this is B12 deficiency. Now, if it wasn't, then you could conclude that it was very likely to be folate-deficient.

Q. Did your opinion change, your medical opinion?

A. It changed, I would say—it changed gradually but certainly within a few years. I knew at this time that other—some labs were ordering single homocysteines. There wasn't anything I could do about them; but I felt for my laboratory and I hoped for Roche that they would offer at least the MMA and the homocysteine together, at least until these tests became more widely used and doctors understood how to use them.

Q. And were there any other developments that prompted a change in your medical opinion?

A. Well, again, it was primarily physician education. Another major change, though, came in the beginning in the mid 90's but really accelerated once, as Dr. Stabler testified, we showed that oral cobalamin was as or more effective than the shots. Now for the first time, a doctor could get the total homocysteine. And if the doctor wanted to, he didn't have to

order other tests or figure out which of the two vitamins was deficient; he could just prescribe a pill that had both a large amount of cobalamin and folate.

Q. Do you have any evidence to suggest that there was the confusion you've described during that time frame?

A. Yes. I think you'll see that in the next exhibit, 144.

Q. What is this exhibit, Doctor?

A. This is a fax that I sent to Dr. Wentz on August 25 of 1992, and it contains the second page is an article from the Wall Street Journal, August 19. And the Wall Street Journal article is noting an article that was published in the Journal of American Medical Association on August 19 of that year. The Journal of American Medical Association article was one that described an association between homocyst(e)ine, with the E in it. If we look at the third page of the exhibit— .

MR. WHITEHAIR: If I could, your Honor, Bates No. L00029.

THE WITNESS: I might just point out that this way of writing homocyst(e)ine was a shorthand expression for total homocysteine. You'll see that in many different articles. And it indicated that in a U.S. physician study, doctors in this country that were in the very top part of the range for homocysteine had a moderate but significant increased risk of having heart attacks. And the point of sending this to Dr. Wentz can be seen if we come back to the second page—

MR. WHITEHAIR: For the record, your Honor, L000028.

THE COURT: Why don't you just give the last 4 numbers. That's easier.

MR. WHITEHAIR: Thanks.

THE WITNESS: Okay. And if we look at the left-hand column, we'll see the article is entitled, "Certain Amino Acid Increases the Risk of Heart Attacks." And if we come down in the article to the third paragraph, it starts out, "But the risk can be offset by dietary supplements of vitamin B6 or a

related vitamin called folic acid, which help metabolize homocysteine." And it refers to Dr. Stampfer, who is a Harvard professor. And this was exactly what I was worried about in the previous letter of doing a total homocysteine. Here you have a medical article in a widely read journal talking about homocysteine and vascular disease, talking about treating with B6 and folic acid and not mentioning treatment with vitamin B12 or the dangers that could occur if you treat it, a B12 patient with folate. And if you'll recall, by this time, Dr. Stabler's elderly studies, we knew there were probably 20 million elderly people in this country that were B12-deficient.

BY MR. WHITEHAIR:

Q. Did Dr. Wentz follow-up with you?

A. Yes. The next Exhibit, 145, is a memo he sent me, again sort of responding to the article that I had sent him, suggesting that they would like to offer a—just a single homocysteine test for vascular disease; that the warning would be that if the—we're talking now about this Bates No. M1000. And if we come down and look at the—what's present in bold, the note, the second sentence, it says "If, however, the test was ordered to evaluate any unexplained hematologic abnormality, a normal or abnormal result is not conclusive. And it is recommended to order the complete megaloblastic anemia profile and then cites this article that I thought was an important article for homocysteine and vascular disease, but it was a dangerous article. And I followed up by calling Dr. Wentz and telling him that I thought this kind of note was far from sufficient; that if you wanted to offer, and they certainly could offer, a single homocysteine, but they certainly needed a much stronger warning to warn doctors that it could be extremely dangerous to treat a patient with an elevated total homocysteine with folic acid and not be aware of the important benefits from B12.

Q. What's time frame of this letter?

A. October 30, 1992.

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[Page 875, line 8 to Page 876, line 8]

THE COURT: I'm having trouble hearing you. I'm sorry. They're paying on the panel test is what he's saying.

MR. HIGGINS: We're paying on the panel test. Basically, what the plaintiffs are trying to argue is that LabCorp pays on the panel test which has a homocysteine test on it; therefore, they ought to be paying on the single test. And we went through that issue on summary judgment, and it's—it should not come out here in this trial. It's not relevant.

MR. WHITEHAIR: It goes to a different issue, your Honor. We know in this correspondence the LabCorp admits they correlate—that they are correlating in Claim 18. And then all we're saying is if they understand the term "correlating" for Claim 18, there is this exact same quotation, correlating in Claim 13, so it's just a use of knowledge of what LabCorp understood. Goes to at least to willful infringement issue.

MR. HIGGINS: Your Honor, Claim 13 doesn't even have—doesn't have a correlating step in it and it doesn't—

MR. WHITEHAIR: That's what the second step is.

MR. HIGGINS: Claim 18 is one step claim. It doesn't have a correlating claim. And this letter was written before your Honor's interpretation of what Claim 13 meant.

THE COURT: Basically, what my ruling was is that you can't patent an idea. You have to patent an act or the test, and really that's about all my ruling was, so I'm not sure I understand what the—where you're going or what the problem is.

* * * *

[Page 881, line 22 to Page 883, line 4]

Q. What was your understanding of what was communicated very generally to LabCorp in that '99—July, '99 time frame?

A. The main thing it concerned was the very strong concern I had about the dangers to patients from adding this message. This is 165A, in which they told doctors not to use the single homocysteine for the diagnosis of B12 or folate deficiency. This was absolutely unbelievable to me. I realized that the vast, vast majority of doctors would look at this and say, "Huh? This is ridiculous." I mean if I have an elevated value for total homocysteine, I've already detected B12 and folate deficiency; and I think they would ignore it and go ahead and either treat the patient or do additional tests if they wanted to pin down which vitamin was deficient. But I think there would be a very small number, maybe no more than 1 percent, that would look at this and say, "Oh, I thought that if I got this as a risk factor for vascular disease or some hematologic problem—I thought that if it was elevated, this would help me diagnose B12 and folate deficiency. But I guess I must be mistaken." And so in those—you know, 1 percent is a small number; but if you're doing 50- or 100,000 tests a year, that means you're talking about 500 or a thousand times when a doctor is looking at this report trying to decide what to do. And in this small percent, if you're the patient, even one is a big number. The patients were being undiagnosed and not treated with the appropriate vitamin. We've already heard this week just how serious that can be. So that was the major issue that we raise the with our communication with LabCorp. We also pointed out that making somebody order a four-test panel and a second homocysteine when you already had the homocysteine we thought was—that wasn't medically dangerous but it was very unfair to patients, people that were going to pay for this, including insurance companies and the government.

* * * *

[Page 905, line 4 to Page 908, line 5]

Q. Did we discuss earlier today your contacts with Abbott?

A. Yes, we did.

Q. Do you have any documents relating to that?

A. Yes, I do.

Q. Let me turn—is it Exhibit 205 in the book—not the one we set down but the one before that.

A. Yes, it is.

Q. What is this document?

A. This is an article that was published by Dr. Shipchandler—Shipchandler, the individual that visited us, published in Clinical Chemistry and is about the fully automated measurement of plasma homocysteine with the Abbott IMX. That's their machine analyzer.

Q. When did you say it was published?

A. 1995.

Q. Is there a reference to your lab on the first page?

A. Yes, If you look on the right-hand side, under "materials," if you come down about six or seven pages "Clinical serum samples were provided by R.H. Allen of the University of Colorado." These were samples with elevated levels of total homocysteine from patients with B12 and folate deficiency.

Q. Is there another reference to Allen on the next page?

A. Yes. In the right-hand [illegible], if we come down till we get to something called [illegible]on parallelism," and if we just go back up three sides, it talks about gas chromatography mass spectrometry and it gives an equation, the correlation between 21 of our clinical samples and the Abbott assay.

Q. Is there a citation?

A. Yes, there is. It is No. 19.

Q. And where is that found?

A. It's found on the last page—well, there are two articles here. It's 81713. And in the right-hand column, three quarters of the way down, it's the Stabler et al. article. This is our article in which we describe our GC mass spec method for total homocysteine.

Q. And what's the—what's this article saying?

A. Well, I think the punch line of this article can be found if we go to the left-hand column, and in this paragraph that says, "We conclude," and come down about six lines.

Q. Let me ask you—excuse me.

A. Yeah.

Q. Is there a reference to the study?

A. Yes. I'm sorry. If we go back up a little bit. Let's go to the left-hand column of this page. Let's come down to where we're starting a new paragraph with "hyperhomocystinemia," and let's go to the second sentence: "In a recent study of 1100 elderly patients Selhub, et al., concluded that 29.3 percent of the cohort exhibited hyperhomocystinemia with 67 percent of this being associated with one or more manifestations of vitamin B deficiency." And the vitamins in this study were folate, B12, and B6. And then if we go on to the important conclusion of this paper, we're now into the next paragraph, about six lines down with, where it says: "The lowering of plasma homocysteine concentrations in hyperhomocystinemia by simple and inexpensive vitamin therapy may lead to intervention not only in elderly patients but also in the general population, with potentially concordant reductions in mortality and morbidity from cardiovascular diseases. An accurate, precise, and automated method for quantifying total homocysteine will help identify patients who might benefit from the intervention." Abbott knew from the very beginning, three years before they actually introduced this assay into the market, that this assay, as total homocysteine assays are - - are all about elevated homocys-

teine, deficiency we now know of B12 and folate, and their treatment for vascular disease and a whole lot of other conditions.

Q. Did Abbott prepare some materials for—I'm sorry.

A. I don't know if you want me to finish this exhibit. There is a second copy of this—

Q. Oh, I'm sorry. You're right?

A. —article. It starts with M81714. And the importance here—it's the same article we just went through. But if you look up in the upper right, there is a note that says, "Dr. Stabler, with compliments of the authors. Thank you for your help, Mohammad Shipchandler."

* * * *

[Page 937, line 1 to Page 938, line 7]

BY MR. WHITEHAIR:

Q. Doctor, do you have, based on what you described—Can you give us a review of the exhibit we've already looked at, Exhibit 165A, LabCorp report of apparent results?

A. Yes. I have this. This is a patient report that LabCorp started using in May of 1999.

Q. Would you read the section that you're going to refer to so that the record is clear.

A. Yes. And I might say that this report, to my knowledge, is still in existence today. It says, referring to the total homocysteine test: "This test is intended to be used as an independent risk factor for vascular disease and is not intended for the diagnosis of folate or vitamin B12 deficiency. LabCorp has available the megaloblastic anemia profile serum for that purpose."

Q. And what's your view of the accuracy of that statement?

A. Well, as I think we've learned, an elevated homocysteine is a marker for much more than vascular disease. It's a marker for B12 and folate deficiency, which in turn is related to Alzheimer's disease, birth defects, toxicity from anticancer drugs, the development of cancer. It's really—it's a marker—it's a risk factor for death from various manifestations of B12 and folate deficiency. And to indicate to physicians that it's only related to vascular disease, particularly not pointing out that the people at risk with vascular disease are the people that already have it, not people that don't, and to indicate—Again, most doctors won't be fooled; but even 1 percent or less of doctors, to fool them such that patients with elevated total homocysteines, which are clearly due to B12 and folate deficiency, I believe is very dangerous.

* * * *

Robert Allen—Cross

[Page 969, lines 3-6]

Q. And from May of '94 to July of '98, LabCorp performed that single homocysteine test using the GC mass spec method that's disclosed in the patent; correct?

A. That's correct.

* * * *

[Page 970, line 25 to Page 972, line 4]

Q. Now, you're aware in August of '98, LabCorp began performing the single homocysteine serum test using the Abbott method; correct?

A. That's correct.

Q. And that method doesn't use gas chromatography mass spectrometry, does it?

A. It does not.

Q. It's not covered by Claims 1 through 12 of the patent; correct?

A. That's correct.

Q. And you're aware that LabCorp continues to perform a single urine homocysteine test by GC mass spec; correct?

A. I'm aware of that, yes.

Q. And LabCorp continues to pay you royalties on that single test done by GC mass spec; correct?

A. Yes.

Q. And LabCorp continues to perform the four-panel metabolite test, which we looked at a report up here for, by GC mass spec; correct?

A. Yes.

Q. And they continue to pay you royalties for that test?

A. That's correct.

Q. And that's the test that—the GC mass spec test or the test that LabCorp uses some of your software that—or technical know-how that you gave them early in the relationship; correct?

A. That's correct.

Q. And they don't use that—that software or robot to perform the Abbott test, do they?

A. I don't believe so.

* * * *

[Page 977, line 4 to Page 982, line 1]

Q. Dr. Allen, is it Metabolite's position that Metabolite is entitled to a royalty on every single homocysteine assay where the result of the assay is less than 13.9?

A. Well, it's Metabolite's position that virtually with a few incredibly rare exceptions that virtually every total homocysteine test that's done in the United States today is

for the purpose of detecting a deficiency of B12 or folate and that as Judge Weinshienk has defined correlating, there are two parts to it. It means to establish a reciprocal or a mutual relationship. And every time a total homocysteine is done, again, with these few very rare exceptions, the physician then either establishes in the physician's mind that there is a mutual relationship between an elevated level and a deficiency of cobalamin or folate, or that there is this reciprocal relationship between an unelevated value and the absence of cobalamin or folate deficiency.

Q. Trudy, put up Claim 13 again, please.

Where in that claim does it say unelevated value and absence of a deficiency?

A. That's what "correlating" means. There is no laboratory test that either an elevated level or a low level, only then do you get information. Every laboratory test, abnormal results give you information and normal results give you information. That's the meaning of what "correlating" means. It's this mutual relationship, and it's a reciprocal relationship.

Q. Dr. Allen, read the second step of Claim 13.

A. "Correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate."

Q. You didn't say correlate an unelevated level with an absence of a deficiency of cobalamin or folate—" did it?

A. It says "correlating." And as I understand it, Judge Weinshienk has stated what "correlating" means. And that means—I may be off a touch on the language, but I think her ruling was it means to establish a reciprocal or a mutual relationship. And that's exactly what correlating means in medical practice.

Q. Dr. Allen, the only term relating to elevated or unelevated in that claim is elevated; correct?

A. The word "correlating," correlating an elevated level; and that means just what I I've testified it means.

Q. It means you have to have an elevated level to correlate, does it not?

A. No, it does not. That's not what correlating means. It means to establish a mutual or a reciprocal relationship. I've never heard of a situation where anyone said that a test was only useful and provided information when it was high or low.

Q. Dr. Allen, you understand that the Court also said that the—strike that.

The Court said that correlating meant to establish a mutual or reciprocal relationship with a deficiency of cobalamin or folate; correct?

A. That sounds familiar. If we're going to get real precise, probably would be helpful to show me exactly the words that Judge Weinshienk used.

Q. Well, do you understand that—

THE COURT: We may need the order, because I can't remember the exact wording. It was a long time ago.

I'm not sure you really need [t]o go into this. When the jury gets instructions on the law, this will be explained to them, unless you need to ask him the question.

MR. HIGGINS: Well, I can move on then, your Honor.

THE COURT: Go ahead.

BY MR. HIGGINS:

Q. Let me ask you, Dr. Allen: Do you understand that the second step involves a discrete sequential step from the first assaying step? You understand that from the Court's order?

A. I understand from the order that it's a, you know, a different step and you can't do it at the same time, yes.

Q. Now, what act falls within the second step? What does a person have to do to fall within the second step of Claim 13?

A. Well, I think—

MR. WHITEHAIR: Objection to the extent it's calling for a legal conclusion.

THE COURT: All right. Of course, he can't answer as a legal conclusion. He can state his understanding, however.

MR. WHITEHAIR: Thank you.

THE COURT: If that's what you're asking.

MR. HIGGINS: Yes, your Honor. I'm trying to find out what someone has to do to infringe. That's the purpose of the claim.

THE COURT: Go ahead. Ask your question.

BY MR. HIGGINS:

Q. Dr. Allen, what does a person have to do to fall within the second step of Claim 13, your understanding as a physician and the inventor?

A. Well, as I understand Judge Weinshienk's ruling, a physician establishes a reciprocal or mutual relationship. Again, I'm struggling to remember the exact language of her claim [sic], but I understand that's what we're using in this case.

Q. Well, what specific act does the physician do to establish that mutual or reciprocal relationship?

A. The physician takes the value that's been determined by the assay and then based on everything the physician knows about that patient, he or she establishes a mutual relationship between an elevated value if the patient—if the

physician thinks the value is elevated for an individual patient and a deficiency of cobalamin or folate, or if the physician believes that for that particular patient the value is not elevated, then that physician in their mind establishes that there is not a deficiency of cobalamin or folate.

Q. And it's all done in the mind?

A. I think so, yes.

Q. And again, where in Claim 13 does it [say] establish that there is not a deficiency of cobalamin or folate?

A. That is the meaning of the word "correlate."

Q. That's Dr. Allen's meaning of the word "correlate"?

A. No, that is Judge Weinshienk's meaning, and it's the meaning of physicians throughout the United States. That's how we interpret laboratory tests.

Q. So it's your testimony that the discrete step of Claim 2 is the mental process in a physician's mind?

MR. WHITEHAIR: Objection to the extent that calls for a legal conclusion.

THE COURT: The objection is overruled. He may answer based on his understanding, not a legal conclusion.

THE WITNESS: Well, I think that's true. I guess as we're talking the question is could someone establish that in writing someplace? I suppose. I don't know whether that would be correlating or teaching correlating; but certainly as physicians practice medicine, this is a step that takes—that is performed by the physician in the physician's mind. Other people might be able to do the same thing.

* * * *

[Page 982, line 15 to Page 983, line 20]

Q. And you recall that initially you filed a Claim 13 to cover an assay for any elevated level of total homocysteine; correct?

A. That is not correct.

Q. Trudy, put up Exhibit MB. And if you would, blow up the top part of it, the first claim. Dr. Allen, if you would, read Claim 13 as originally filed and rejected that's shown on Exhibit MB.

A. Yes. "A method for detecting a deficiency of cobalamin or folate in warm-blooded animals by: assaying body fluids for the presence of elevated levels of total homocysteine."

Q. And in response to that—that claim as filed, the examiner rejected it, saying that the preamble was just a statement of intended use. Do you recall that?

A. I recall that that's how the examiner interpreted that statement. That was perfectly proper for the examiner; but as I testified earlier, our intent was clearly to limit this claim for detecting a deficiency of cobalamin or folate. And if we weren't going to limit it to that, that wouldn't even have been put in there. We would have just said Claim 13, assaying body fluids for elevated levels of total homocysteine. We didn't put that in. We clearly put what we thought was a limitation.

Q. So you agree that Claim 13 doesn't cover a method of monitoring and screening for risk of heart disease by assaying serum total homocysteine; correct?

A. I do not agree with that. I think that is absolutely false, because it's cobalamin and folate deficiency that's responsible for the risk and for the vascular events and that doctors in this country know that. And when they order this test for a patient with vascular disease, they're trying to find out if the patient is cobalamin or folate deficient so they can treat patients for those deficiencies.

* * * *

Dr. Kilmer McCully—Voir Dire

[Page 1025, lines 12-16]

Q. Are you an expert in B12 and folate?

A. I would not say so. I would say I have a knowledge of this area, but this has not been my primary field of concentration. My primary field of research has been homocysteine and vascular disease.

* * * *

[Page 1026, lines 14-17]

THE COURT: At this time, the Court is satisfied that Dr. McCully may be helpful to the Court and Jury and will accept him as an expert or opinion witness in the science and medicine of homocysteine.

* * * *

Dr. Kilmer McCully—Direct

[Page 1063, line 16 to Page 1067, line 17]

Q. And can you quantify how many elevated levels of homocysteine in the general population would be attributable to renal disease or B6 deficiency or these other causes or B12 deficiency or folate deficiency?

A. This question has not been examined in detail. The one study that comes to mind that has tried to answer this question is the Framingham heart study, in which they analyze the dietary intake of these three B vitamins, related them to the plasma levels and also the level of homocysteine. And what they found was that in a group of elderly participants—these are individuals between the age of 65 and 93—that approximately a third had no evidence of vitamin deficiencies or elevation of the hornocysteine; but about two-thirds of this group had some evidence of deficiency of one

of these three B vitamins. And when deficiency was present, they found an elevated level of homocysteine.

We know that renal disease is very common in this age group, also; and so I've estimated that perhaps as much as—perhaps as much as 50 percent of the individuals with elevated homocysteine may have some other cause than dietary deficiency.

Q. So if all the renal disease and hypothyroidism and these other factors that you mentioned—they account for approximately half of the elevated levels of total homocysteine, in your opinion?

A. As much as that. It's difficult to be certain of the exact figure, but a significant fraction will have these other causes.

Q. Now, do you have recommendations--do you have a recommendation for what someone should do if their homocysteine is elevated?

A. Yes. As explained in my earlier articles and also my recent books, I believe that the first line of therapy should be dietary improvement. And this is in my opinion an extremely important way to improve and preserve health; that one of the benefits of improving the diet will be to lower homocysteine levels. And the reason of this—for this is manyfold. First of all, an optimal diet, such as my heart revolution diet, recommends eating fresh vegetables, fresh fruits, fresh seafood, meats, whole grains, and so forth, to provide in the food an optimal level of all micronutrients, including the three vitamins that we've been discussing.

But such things as antioxidants and fiber and vitamins, like fat-soluble vitamins, are all important to good health. And by improving the overall diet, this is the best way in my opinion to preserve health and prevent vascular disease. And I've been a consistent advocate of this for many years.

In the case where dietary improvement has been carried out for some months or years and one still observes elevated homocysteine levels, I think there is a case for adding supplemental B vitamins to help control the level of homocysteine with the hope of preventing vascular disease.

Q. And when you say supplemental B vitamins, which B vitamins are you referring to?

A. Well, the three B vitamins that control homocysteine levels are B6, B12, and folic acid. These are the three that I emphasize because of their direct controlling function in the level of homocysteine.

And in my recent book, I give a table in which I relate the levels of homocysteine and the risk of vascular disease to the recommended intake of the supplemental vitamins in addition to dietary improvement.

Q. And Trudy, if you'd put up Exhibit BE.

Dr. McCully, do you recall this Wilcken article dated 1981?

A. BE?

Q. BE. Do you recall we discussed—

A. Yes, I do.

Q. —before the break and—

A. I have it.

Q. —and there was a Figure 2 in that article.

Now, does that article support your position or opinion that supplemental B12, folate, or B6 will lower homocysteine?

A. Yes.

Q. And when you first were involved in this field, what B vitamin did you focus on in the beginning?

A. I focused primarily on vitamin B6. The reason for that was that the important studies of Rinehart in B6-deficient monkeys were a direct—directly related homocystine to arteriosclerosis, in my view.

In addition to that, the patients—most of the patients, or many of the patients with homocystinuria respond to vitamin B6 therapy. About half of the most common form of patients with homocystinuria respond to B6 therapy by lowering of the homocystine level and also improvement in development, prevention of disease, and prevention of vascular disease.

So—and other reports that I found in the literature relating B6 deficiency to vascular disease—these were the reasons that I focused on the relation between homocystine and vitamin B6 in my earlier studies.

Somewhat later, other investigators, some of whom we've discussed today, began to focus more closely on folic acid and vitamin B12.

In fact, when I was first investigating this—this theory in 1968, I examined a series of cases from our files at Massachusetts General Hospital of cases of pernicious anemia, of patients who had died before liver therapy was introduced in the 1920's. Unfortunately, I was not able to document any evidence of vascular disease in these patients, so I left it to other investigators to explore this area, which I felt was important but was beyond my capability at that time.

* * * *

Dr. Kilmer McCully—Cross

[Page 1068, lines 4-24]

Q. Total homocysteine, homocystine, homocysteine—they sound similar, don't they?

A. Yes.

Q. They're not the same, are they?

A. No. It's confusing, I know.

Q. Homocystine, in fact, is one of the several species that make up total homocysteine; correct?

A. Correct.

Q. Okay. As you went through the many exhibits and many articles shown to you by Mr. Higgins this morning in the fat notebook, did you find a single one that measured total homocysteine in a B12 or folate-deficient patient?

A. The disulfide, you're referring to?

Q. No, I'm referring to total homocysteine.

A. Okay.

Q. The collective species, all of them together.

A. Did I find them in here? I mean—

Q. Did you find anywhere in the notebook of articles an article before 1986 that measured total homocysteine in a B12-or folate-deficient patient?

A. I don't believe so, no.

* * * *

[Page 1083, line 22 to Page 1084, line 9]

Q. That's in fact exactly what you did on yourself, isn't it? You had a—a total homocysteine test done on yourself?

A. Yes.

Q. And not MMA test?

A. No.

Q. And you found that the level was something higher than you would like it to be?

A. Yes.

Q. So you took both vitamins?

A. Well, I went on a large-scale program of dietary improvement and—

Q. And that includes the ingestion of more B12 and folate?

A. But I also took multivitamins, yes.

* * * *

[Page 1085, line 7 to Page 1086, line 2]

Q. In your books, do you recommend that the reader have his MMA checked?

A. No.

Q. But you do recommend that he have his total homocysteine checked?

A. Yes.

Q. And if the reader finds that his total homocysteine is high, you recommend that he ingest more B12 and folate; right?

A. Well, I recommend that he be evaluated by a physician to determine the cause of his elevated homocysteine. A thorough history, physical examination, thorough evaluation by a competent physician to determine the source of the elevated homocysteine. That's the first step. The second step, I recommend dietary improvement. And I have a series of chapters and plans for how this can be done to eat The Heart Revolution diet. And then I say in the book that if—if there is no other cause for the elevation of the homocysteine and if dietary improvement does not succeed in lowering it to an optimal level, then I suggest that the patient should consider taking supplemental vitamins, including folate and B12.

* * * *

[Page 1096, line 15 to Page 1100, line 10]

Q. Do you recognize this as the LabCorp Directory of Services that we discussed before the lunch break?

A. Yes.

Q. Could you please turn again to the same page we were on before, which is labeled L324 in the bottom right-hand corner. Do you see in the left-hand column the same test that we focused on before, test 706994 for homocysteine, plasma or serum?

A. Yes.

Q. Do you see the heading "related information"?

A. Yes.

Q. And do you see the reference to "anemia profile megaloblastic, serum"?

A. Yes.

Q. You would not have been aware of this cross-reference in this test at the time you signed your report because you had not been furnished this Directory of Services; correct?

A. That's correct.

Q. Look on down, if you would, please, to the heading "use" about three quarters of the way through that test and just about midway on the page in the left-hand column. Do you see it?

A. Yes.

Q. Do you see the sentence, "Evaluate borderline folate deficiency as part of anemia profile megaloblastic, serum test"?

A. Yes.

Q. Do you interpret that statement to mean that the use of this test is to evaluate borderline folate deficiency along with another test?

A. Yes. I assume there are other tests in the anemia profile and that this is part of it.

Q. Do you see the heading "references," which is the last heading under the description of this test in the Directory of Services?

A. Yes.

Q. Do any of the articles that are under the heading "references" describe to the reader the correlation between elevated homocysteine and B12 or folate deficiencies?

A. Could you repeat the question?

Q. Do any of the articles listed under the heading "references" in the description of this test describe to the reader the correlation between elevated total homocysteine and B12 or folate deficiencies? If it would be helpful to review the articles, I can make them available to you.

A. I believe the Ueland article in Clinical Chemistry addresses this question, as I recall. I'd have to review it to be certain.

Q. Could I ask you to look at a copy of the Ueland article in Plaintiff's Exhibit 185 so that you could determine that.

A. Yes.

Q. Okay. Ueland does teach to the reader the correlation between elevated homocysteine and B12 and folate deficiencies?

A. Yes.

Q. And that's one of the several articles listed under "references" in the description of the test. What about the Malinow article? Do you see that under the heading "references"? And if it would help you in answering my question, which I would anticipate will be the same, you might look at Exhibit 188. While you're looking at that, just to be clear for the record, the question again is: Does the Malinow article describe to the reader the connection between total homocysteine and B12 or folate deficiencies.

A. The article focuses on arterio-occlusive diseases, and the discussion of the concentrations of the homocysteine refer to the correction by folic acid with pyridoxine, vitamin B12, choline or betaine.

Q. Is the answer to my question no, then?

A. It doesn't address the—the article doesn't address your question directly. It does indirectly.

Q. What do you mean by indirectly?

A. It discusses, as mentioned in the summary, that the increased homocysteine concentrations associated with coronary disease can be corrected by folic acid, pyridoxine, B12, choline, or betaine therapy.

Q. So it does teach that elevated levels of total homocysteine –

A. Yes.

Q. —are correctable with B12 and folate?

A. Yes.

Q. Okay. What about the Robinson article, which is also listed under the heading "references"?

A. Which one is that?

Q. That is Plaintiff's Exhibit 187.

A. Yes, it does address the—the answer to your question is yes.

Q. What about the Verhoef article, also listed under the heading "references"?

A. Which one is that?

Q. Plaintiff's Exhibit 186.

A. Yes. This addresses the question of vitamin deficiency in relation to elevated homocysteine levels.

Q. Thank you.

* * * *

[Page 1103, line 21 to Page 1105, line 8]

Q. Back to the form of patient report, which is Exhibit 165A. Do you see in the right-hand column about a third of the way down a paragraph beginning with "this test"?

A. Yes.

Q. And it goes on to state: "This test is intended to be used as an independent risk factor for vascular disease and is not intended for the diagnosis of folate or vitamin B12 deficiency." Is that how you read it?

A. Yes.

Q. Now, if a patient does have elevated total homocysteine, you say in your books that's a bad thing, don't you?

A. Yes.

Q. And elevated total homocysteine is indicative of a need for additional B12 or folate, is it not?

A. It can be.

Q. So if a patient has elevated total homocysteine, shouldn't something be done about that?

A. Yes.

Q. You testified before lunch, I believe, that armed with a patient report only, showing an elevated level of total homocysteine, a physician can't tell for sure that the patient is deficient in B12 or folate. Have I paraphrased you well?

A. That's correct.

Q. But armed with a patient report showing elevated total homocysteine, the physician will know that it's more probable that the patient is B12 or folate-deficient than if the—if the physician is not armed with that report. Isn't that fair to say?

A. Yes.

Q. So it's a matter of probabilities; right?

A. Yes.

Q. Isn't that what it means to correlate? It's not a matter of certainty, is it? It's a matter of probabilities.

A. To correlate is to—is to relate one finding to another.

Q. But not necessarily with certainty but only with probabilities?

A. Not necessarily—that's correct.

* * * *

[Page 1110, line 15 to Page 1111, line 20]

Q. Let me ask you to consider a hypothetical question, if I may, since you've been qualified as an expert for a limited purpose. Let's assume for a minute that your theory is right. It hasn't been proven, but let's assume that for the purposes of argument elevated total homocysteine indeed causes vascular disease; okay? And let's assume further for purposes of argument that your theory is not only right but some physicians believe it is right. And so some physicians indeed order total homocysteine tests for their patients in order to assess their risk for vascular disease. Okay? You're with me in my set of assumptions?

A. Yes.

Q. If all that's true and a total homocysteine test for the physician's patient comes back elevated, then the physician should conclude, according to your theory, that the patient has a heightened risk for vascular disease; am I right?

A. That's correct.

Q. Because a heightened risk for vascular disease in an effect of elevated total homocysteine, you theorize?

A. That's correct.

Q. Well, even assuming that all that were true, that doesn't address the treatment side of the equation, does it?

A. That's correct.

Q. Shouldn't the physician in those circumstances also be concerned about the treatment for this elevated total homocysteine?

A. Yes.

Q. And in your professional experience, physicians indeed normally are concerned about the treatment - -

A. Yes.

Q. —of conditions.

* * * *

[Page 1111, line 21 to Page 1113, line 9]

Q. Dr. McCully, could you look at Defendant's Exhibit A, please.

A. Oh, yes.

Q. Do you recognize this as the patent at issue in this case?

A. Yes.

Q. And you've reviewed it in the past; correct?

A. Yes.

Q. You're not an expert in interpreting patent claims, are you?

A. No, I'm not.

Q. Leave aside the claims, then. Okay? Apart from the claims, is the language of the patent misleading or inaccurate or untrue in any respect?

A. No. In general, no. There are a few minor typographical errors that I picked up; but aside from that, there are no—no major errors that I found in my reading of it.

Q. These two University of Colorado professors, Dr. Allen and Dr. Stabler, named as inventors of the patent truly are experts in B12 and folate, are they not?

A. Yes.

Q. And Dr. Lindenbaum, the late Columbia professor, was an expert in B12 and folate; won't you agree?

A. Yes.

Q. They've received a lot of recognition for their work, haven't they?

A. Yes.

Q. They've had over a hundred articles published in leading scientific journals?

A. I don't know how many, but I know that there are multiple articles.

Q. They haven't gotten their names in the paper about this, but they've received a lot off recognition from their peers in the field, wouldn't you say?

A. I would say hematologists, yes, have used their findings and to benefit their patients, yes.

Q. Now, the idea that elevated total homocysteine can be brought to save levels by administering B12 and folate is a pretty significant idea, wouldn't you say?

A. It's an important idea, yes.

* * * *

Robert Allen—Cross

[Page 1133, line 17 to Page 1137, line 11]

Q. So you run into situations where someone may read something in a newspaper or magazine or see it on television about a medical test and next time they go to the doctor they ask for it?

A. Well, I would say they bring it to the attention of the doctor and ask questions.

Q. Now, assume a person were to read about homocysteine and the risk of heart disease and goes to their physician

and asks the physician to measure their total homocysteine. Assume that. And assume the level comes back at a 5 and nothing is done. The doctor says, ["]You got a 5."

Now, did the doctor infringe Claim 13 of the patent, in your opinion? Is it Metabolite's position that the doctor infringed Claim 13?

A. Well, I think that's covered by Claim 13, because I think doctors in this country, when they order a total homocysteine, whether it's risk factor for vascular disease or other causes, when the result comes back, they then establish whether there is a mutual relationship between an elevated level and a deficiency of cobalamin or folate, or whether the reciprocal relationship is present[]; namely, the value is not elevated and there is no deficiency. That's the way Judge Weinshienk has defined the word "correlate," and I think physicians do that. And I think a physician that looked at a value of 5 would—would very, very, very likely decide that there was a reciprocal relationship in this particular patient between a non-elevated level and an absence of cobalamin or folate deficiency.

Q. What discrete sequential step did the doctor perform that falls within Claim 13?

A. The step I just explained. He did the correlate step.

Q. And what exactly did the doctor do?

A. Well, I think I just answered that. The doctor looked at the value of 5, and I think it's extremely likely with a value of 5, if there was no other information present, no prior values, the doctor would have established that there was a reciprocal relationship between this almost certainly or incredibly likely non-elevated value and an absence of cobalamin or folate deficiency.

Q. Trudy, put up Exhibit 26.

Dr. Allen, read—now, this is the claim chart that the plaintiffs have prepared for this litigation; correct?

A. That's correct.

Q. If you would, read the last sentence or—strike that—the last phrase after "and."

A. "To establish a mutual or reciprocal relationship between a level of total homocysteine raised above the normal range in said body fluid with a shortage of cobalamin or folate necessary to health."

Q. Now, the 5 in my hypothetical is not raised above the normal range, according to your patent, is it?

A. I think we went through this the last time I was on the stand. A 5, it is incredibly unlikely that that is elevated above the normal range.

Q. And the second step requires a correlation of an elevated level with a deficiency; correct?

A. Well, it says, as Judge Weinshienk has defined the word "correlate," it means, quote, "to establish a mutual or reciprocal relationship between a level of total homocysteine raised above the normal range in said body fluid with a shortage of cobalamin or folate necessary to health."

Q. And the 5 is not raised above a normal range; correct?

A. It is possible, but it is extremely unlikely.

Q. And for any particular result of a single homocysteine test that's—well, strike that.

Well, let me ask you: Does the patient in my hypothetical—did the patient—what the patient did fall within Claim 13?

A. You mean asking the physician to consider ordering a total homocysteine test?

Q. Yes.

A. I don't think just asking for a total homocysteine test, that act all by itself—I don't think it does.

Q. What about receiving a result from the physician—asking and receiving a result from the physician? Is it Metabolite's position that that would infringe Claim 13?

A. Well, I suppose—I think it's very unlikely that a patient would get a test and the doctor would just give them the result, but I think patients that would go to the doctor and ask for a total homocysteine are very likely to have an understanding of what the result might mean.

Q. So is it Metabolite's position and CTI's position, to your knowledge, that a patient asking a physician to perform total homocysteine test and receiving the result would infringe Claim 13?

A. Well, I—we have LabCorp doing the test, the physician ordering the test. Somebody, whether it's the physician or the patient, is going to understand how to interpret the test and will perform the correlating step. So somebody will be infringing Claim 13.

And as we've talked about, there are different kinds of infringement. There is inducing and contributory; so in that situation, I think LabCorp would be guilty of contributory, and the physician or the patient would be part of that.

* * * *

Dr. Robert Allen—Redirect

[Page 1225, line 8 to Page 1228, line 8]

Q. Do you recall discussing the issue of total homocysteine as a risk factor?

A. Yes, I do.

Q. What do you understand the argument to be about its use as a risk factor?

A. I think that that argument goes that a doctor will order a total homocysteine on a patient in order to see if that patient is at risk or has an increased chance of developing vascular disease; that once that result is obtained, if it's

elevated, the doctor does nothing more than inform the patient that here's some bad news for you, you're at higher risk for vascular disease than I thought you were before I got the test and, you know—

Q. What, in fact, do doctors do after receiving information on this test?

A. Well, doctors—

MR. HIGGINS: Objection, your Honor. Limited to his knowledge.

THE COURT: All right. Would you restate your question. You're asking him to the best of his knowledge.

BY MR. WHITEHAIR:

Q. To your knowledge—to the best of your knowledge, Doctor, what do doctors--pardon me. To the best of your knowledge, what do doctors do when they receive the test results on a single total homocysteine in a situation where someone considers it a risk factor?

A. Well, they may or may not do additional tests; but in virtually every case, they then end up treating the patient with either cobalamin and/or folate.

Q. Where do doctors learn about that step?

A. Well, they learn about it in textbooks, they learn about it in multiple journal articles, they learn about it from LabCorp in the articles that are listed in the Directory of Services, and they also learn it from articles, continuing medical education articles that Dr. Wentz has written.

Q. Do you recall having it suggested to you that no royalty should be paid if there is a normal result?

A. I have heard statements made that the patent only covers tests where the results come back as elevated, yes.

Q. What is your reaction to that, Dr. Allen?

A. Well, I don't know of any medical test where the information is useful only if it's elevated or low or abnormal.

In every test that I know of, information that the doctor acts on is always obtained regardless of the normality or abnormality of the test result.

Q. And what's the analogy that you use in your practice?

A. Well, the analogy that I touched on in my earlier testimony was a pregnancy test. If the pregnancy test comes back as positive, then the doctor correlates. We always correlate with any test result. In this case, the doctor would establish that there is—would know that there is a mutual relationship between a positive pregnancy test and a woman being pregnant and then would obviously act on that to make sure the patient received care throughout pregnancy and afterwards.

Q. And what about the opposite result?

A. Well, if the pregnancy test is negative, then that's the reciprocal. A negative test indicates no pregnancy, and the doctor would act on that. It would make a difference whether the patient wanted to be pregnant or not. If the patient did want to be pregnant and the patient had been trying for a long time, there might be various fertility treatments or things that might be done. If the patient did not want to be pregnant, then the doctor might inform the patient about various birth control options.

Q. Is this analogy you're describing applicable to the total homocysteine only test?

A. Yes. I think it's applicable to every test. Doctors, when they order the total homocysteine test and when it comes back, as I've testified repeatedly, they always correlate. If it's elevated, it's the mutual relationship with cobalamin or folate deficiency. If it's not elevated, it's the reciprocal or absence of cobalamin or folate deficiency. They act accordingly with each result, depending on the patient—

Q. I'm sorry.

A. I was just going to say depending on the individual patient.

* * * *

Peter Wentz—Direct

[Page 1244, line 10 to Page 1245, line 9]

Q. Let's talk about your role in the LabCorp Directory of Services, if we may. What is the Directory of Services?

A. The Directory of Services is a publication produced by Lexi-Comp. It includes tests that are published tests that are provided by LabCorp to our clients, so it's a listing of those tests.

Q. So it's a listing and description of the tests that LabCorp makes available to its customers?

A. Yes.

Q. Does it come in book form?

A. Soft copy. There is a few hard copies, but most of them are soft copy, hard copy.

Q. Something I could pick up in my hands; right?

A. Yes.

Q. But a pretty big thing that I'd pick up in my hands; right?

A. Fairly thick.

Q. Like a phone book?

A. A local phone book.

Q. It's also accessible on line, is it not?

A. The—yes. We have an on line Directory of Services.

Q. Is the Directory of Services a tool that LabCorp uses to market its tests to physicians?

A. Is it a tool? Used for marketing? There may be some promotional advantage of having it on line. Certainly, we use that tool to educate our physicians and clients.

* * * *

[Page 1314, line 22 to Page 1316, line 1]

Q. Let's go to the patent, if we could. I believe there is copy of it in Defendant's Exhibit A.

A. Thank you.

Q. If you'll look to the second to last page, Claim 13. Now, as you indicated in your e-mail to the Mayo Clinic, Claim 13 covers a procedure in which both the following steps are performed; right? (1) an assay step and (2) a correlating step?

A. I believe that was the gist of my e-mail.

Q. And it doesn't matter whether the test is by GCMS. Correct?

A. I believe that was in my e-mail, yes.

* * * *

[Page 1315, line 9 to Page 1316, line 8]

Q. Now, do you understand the word "correlating" to mean establishing a mutual or reciprocal relationship?

A. Yes. That's been defined by the—

MR. JABLONSKI: I would object to the question, your Honor. The Court has defined what correlating is, and there is no reason for Mr. Wentz to redefine it for the jury.

THE COURT: He may state his understanding. The objection is overruled. Not a legal definition but his understanding.

BY MR. BEATON:

Q. And you've had that understanding all along, haven't you, as to what correlating means?

A. Well, it was defined by the Court. I do have that appreciation, yes.

Q. Was it defined by the Court in a manner different than your understanding?

A. I—I don't recall if it was different necessarily. It was a definition.

Q. Now, LabCorp still does pay royalties on the panel test; right?

A. That's correct.

Q. And LabCorp pays royalties on the panel test still regardless of whether the result is high, low, or in between; right?

A. Irregardless [sic]. That's correct.

* * * *

Peter Wentz—Cross

[Page 1316, line 16 to Page 1317, line 17]

Q. LabCorp does perform the assay step in the panel test; right?

A. Yes.

Q. Is it your position that LabCorp does not perform the correlating step in the panel test?

A. Quite emphatically it does not perform the correlating step. That's a—that's a separate, distinct step that's performed by the physician who receives the—our results.

Q. Could you look at your deposition from January, 2000, page 122.

A. Yes.

Q. Line 24.

"Question: Right. And 706960 falls within the claims of the licensed patent because it includes a correlating

step. That's my question." Before I go on to the answer, 706960 is the panel test; correct, Doctor?

A. I'm sorry. What was your question?

Q. 706960 is the panel test; right?

A. Yes, that's the four-panel test.

Q. Let me start again then. "Question: Right. And 706960 falls within the claims of the licensed patent because it includes the correlating step. That's my question." "Answer: Yes." Did I read it right?

A. Yes, you did.

* * * *

[Page 1418, line 3 to Page 1420, line 13]

Q. All right. I would like to turn now to the—switch to the Abbott test. You remember you were questioned about that by Mr. Beaton, and I want to ask you some additional questions about that. When is it that you at LabCorp first became aware that there was even going to be an Abbott test?

A. It was the same publication that Dr. Allen cited by Shipchandler in 1995 that was an Abbott publication. It appeared in the Journal of Clinical Chemistry. That's my—

Q. What is your recollection of what that said?

A. Well, it described the Abbott method. Basically the same Abbott method that's in use today.

Q. Was the Abbott method commercially available in 1995?

A. Unfortunately not.

Q. When, to your knowledge, did it first become available?

A. Reagents became available, I believe, in the latter part of 1997.

Q. Does a test or kit of the kind that Abbott was proposing to sell require approval by the FDA?

A. Yes. All diagnostic kits must be FDA approved.

Q. What is your best recollection when this diagnostic kit became FDA approved?

A. I think we received a letter in October of 1998 that it had been FDA approved.

Q. And what did that permit LabCorp to do?

A. Well, it permitted us to switch over from bulk reagents, which we were using, to the kit reagents.

Q. You have testified in response to questions by Mr. Beaton that the determination to go forward with the Abbott test was made in August of 1998; is that correct?

A. Well, that's when we implemented it. The determination had been made prior to that.

Q. Approximately when was the determination itself made?

A. It would have been made after we finished our evaluation of the bulk reagents.

Q. Did you participate in that evaluation?

A. Yes.

Q. Tell us briefly what you did.

A. Well, I had to obtain an import license, USDA import license. I had to apply for that because these bulk reagents were coming from Oslo, Norway, from a company known as Axis, A-X-I-S, Chemicals. So I had to go through the whole process of applying for the import license and then—and that took probably four to six weeks. And then once that occurred, then I could place an order for the bulk reagents.

Q. And how did you use those bulk reagents?

A. Well, we used it in an evaluation of the procedure. We had by that time an agreement with Abbott so that they had set up a research, what they called, I think, a research-type instrument in our laboratory.

Q. Was that done pursuant to an agreement with Abbott?

A. Yes.

Q. Okay. And what were you doing during this research phase?

A. Well, we were going through a method evaluation.

Q. And what was your evaluation? How did you like it?

A. Well, the results of the evaluation were that we had accepted it. We accepted that particular procedure.

Q. What were you looking for?

A. Well, we were looking for a method that was at that time faster, more cost-effective, had excellent precision, reproducibility; that is, from not only within a run but from day to day and one that gave good results.

* * * *

[Page 1421, line 6 to Page 1423, line 3]

Q. Who participated in this research or evaluation phase other than yourself?

A. Well, individuals within our laboratory under my direct supervision—of supervisors, techs, chemists.

Q. And what were your conclusions at the end of this period?

A. Well, the conclusion was that we had a good method, the Abbott procedure was acceptable; and we placed it into operation in August of 1998.

Q. What did you see as the advantages?

A. Well, as I mentioned, the big advantage was, I think, reduction in the turnaround time. A procedure that for the single homocysteine that took, oh, upwards of 18 hours to turn out a result now was reduced to a matter of minutes. So as far as throughput, you know, putting samples through the instrument and generating results, the Abbott procedure was far superior to the procedure that we were using.

Q. And what was the procedure that you had been using?

A. That was the GCMS procedure.

Q. And was that the licensed procedure under the agreement with the plaintiffs in this lawsuit?

A. That's correct.

Q. Now, what is the difference between the kit and the bulk reagent?

A. Well, in size, primarily. The kit [sic], I believe, consisted of components, and you had to put the components together, whereas the kit, everything was together. There was no mixing up of reagents. Everything was premixed. All you had to do was place these reagents directly on the instrument, which was the Abbott. There was no preparation involved.

Q. That is a benefit?

A. That's always a benefit. I mean it takes time to prepare reagents. And the Abbott procedure virtually eliminated that phase of it.

Q. Is that procedure helpful in eliminating human error?

A. Well, anytime you can reduce the number of steps in a procedure, you reduce the opportunity for error.

Q. Was it important to LabCorp during this period in 1998 that it be able to speed up its accomplishment of these tests?

A. Yes.

Q. And why was that?

A. Well, I like to use the term critical mass. We had reached critical mass when it came to our single homocysteine testing.

From a period of January of 1997 through December of '97, we had—we had had a 300 percent increase in our homocysteine requests. We went from a thousand a month to 4,000 a month.

On into '98, that number just seemed to skyrocket. We couldn't keep up with the work using GCMS.

* * * *

[Page 1426, line 17 to Page 1429, line 2]

Q. Dr. Wentz, how do you know that in 1997 and 1998 there was a significant increase in the requests for the single homocysteine test?

A. Well, people told me, for one thing, they were having a hard time keeping up with the workload. Plus the numbers were reflected in that report, that workload report I just mentioned, the HLR tot. It's showed basically an exponential increase in the number of requests we had received for the single homocysteine in that time period.

Q. Did that burden you and your technicians at the division where this was being done?

A. That's putting it mildly, yes.

Q. And did you kind of welcome the commercial availability of the Abbott test as a way to deal with that problem?

A. Well, it was an advance in the technology, yes.

Q. Why would you describe it as an advance in the technology?

A. Well, it virtually eliminated all the prep time required to get a sample ready for GCMS.

Q. Is the Abbott procedure essentially automated?

A. Yes.

Q. Now, you were asked some questions about whether you were expert in various and sundry disciplines, and you responded to those. And I want to just return to this matter of homocysteine, if I could.

What did you do after you were assigned or became responsible for the performance of the four-test panel pursuant to the licensing agreement with the plaintiffs to inform yourself about homocysteine?

A. Well, I tried to get all of the materials that I could from the literature. It was a little bit difficult in—I think the early 90's. It wasn't until when I got on line with the national Library of Congress that I could get reports, get directly from Duke University that I was able to get the information that I needed, plus Dr. Allen was—shared a lot of that information with me as well.

Q. Did you by those methods, your own reading and discussions with Dr. Allen, become informed about homocysteine?

A. Yes. I made it a point to become informed.

Q. Now, you have said that you are not expert in homocysteine. That's right, isn't it?

A. I did state that. That's correct.

Q. Okay. And you have not, for example, like Dr. McCully or like Dr. Allen or like Dr. Stabler, you know, sought any grants or conducted any independent research with respect to homocysteine, have you?

A. No, I haven't.

Q. And, in fact, is your position as a manager at LabCorp a full-time occupation?

A. It keeps me busy. Yes, it is.

Q. So would you describe yourself as knowledgeable about homocysteine but not expert?

A. I'd say very knowledgeable but not expert.

Q. Okay. Now, with that said, why, to your knowledge, was there such an increase in demand for these single homocysteine tests in 1998?

A. Well, information was starting to come out that homocysteine was an independent risk factor for cardiovascular disease and thrombosis.

Q. Is cardiovascular disease and thrombosis a common condition, to your knowledge, in the American population?

A. I mean it's the No. 1 killer in the United States.

* * * *

[Page 1482, lines 5-6]

Q. You were here for Dr. McCully's testimony; right?

A. Yes, I was.

* * * *

[Page 1482, line 20 to Page 1483, line 1]

Q. Do you dispute Dr. McCully's testimony that homocysteine testing is not used to detect a patient's age, gender, alcohol intake, smoking status, renal disease, whether he has lupus, whether he has rheumatoid arthritis, whether he has hypothyroidism, or whether he has ingested drugs or toxins?

A. No, I wouldn't dispute that.

* * * *

[Page 1579, line 24 to Page 1580, line 4]

Q. Now, with respect to this range and with respect to the outcomes altogether of the several hundred thousand tests that have been done by LabCorp as a single homocysteine test, how many of them typically are raised above normal; that is, in excess of 15?

A. Less than 20 percent.

* * * *

[Page 1629, line 19 to Page 1632, line 8]

Q. Dr. Wentz, could I ask you to look at Plaintiffs' Exhibit 19.

A. Yes, I have it.

Q. Okay. Do you recognize the quote from the Ueland article: "Thus, the laboratory diagnosis of cobalamin and folate deficiency will probably account for the largest number of plasma serum homocysteine determinations"?

A. I don't recognize it, but I see it.

Q. Okay. The Ueland article is one of the references listed in the homocysteine only test description in the Directory of Services; right?

A. I'm aware of that, yes.

Q. Similarly, do you see the next quote out of the Verhoef article?

A. Yes.

Q. I won't bore everyone by reading each of these. But Verhoef also is an article listed in the references section of the Homocysteine Only Directory of Services; right?

A. That's correct.

Q. Same thing with Robinson—right—the last on the page?

A. Correct.

Q. If you'll flip over to Plaintiffs' 20.

A. I'm there.

Q. Keep going, please, to 21. These are quotes from your article; right? "Homocysteine, the bad amino acid"?

A. I'd have to cross-reference it, I guess, with the actual article.

Q. Okay. Let's not take the time to do that. And on page 2, do you see further quotes?

A. Yes.

Q. And then finally, on Plaintiffs' 22, do you see the quote from your other article, "Megaloblastic Anemia," stating, "The metabolite patterns are characteristic for the particular vitamin involved. These biochemicals pathways have been studied extensively, and the clinical implications have been described in various publications appearing over the course of more than 30 years. Subsequently, the clinical correlations and analytical methodology became the basis for two U.S. patents." And then you see the footnotes two U.S. patents, both by these three professors and the one being the one at issue in this case; right?

A. Yes. I did cite those.

Q. Now, the Directory of Services in which these references appear is used to help educate physicians about the test; right?

A. You're referring to the single homocysteine test?

Q. Yes.

A. Yeah. Those references are there because they support the information described in the test descript[ion]. They're there for that purpose.

Q. And for physicians to refer to; right?

A. Certainly they may refer to it, yes.

Q. And the articles that you wrote are used to help market the tests? Right?

A. Well, that wasn't the primary reason for writing those articles, no. It may have—I mean they make may have a marketing function.

Q. So all of this, the articles and the articl.s that you wrote, are available to LabCorp's customers, aren't they?

A. Certainly they're available through Medline, the Library of Medicine. I mean they are available, yes.

Q. In fact, they're available to the general public; right?

A. Correct.

* * * *

[Page 1689, line 5 to Page 1690, line 6]

MR. HIGGINS: Well, your Honor, on that issue, again the —because of the prosecution history, where the examiner required that second step to be added to overcome the prior art and particularly a 102 anticipation rejection, there is no equivalence on that step. And that recent Festo decision which cert. has been granted on—that decision specifically says where an element has been limited in view of a patentability rejection, then there are no equivalents.

THE COURT: Mr. Higgins, I'm probably going to agree with you on some of these, because with all due respect to Dr. Allen, who I think is a genius on what he has done, it's difficult to think you can patent an idea, rather than a test. And that's what I'm afraid some of these patents do, is try to patent an idea. And there is problems with the wording as far as—this has been, you know, shown to the jury add ad nauseum about the raised homocysteine giving rise to certain conclusions when some of the tests are not raised. However, my experience with patent cases in the 22 years or so that I've been sitting here in Federal Court is that when I try to apply common sense to some of these, invariably I get reversed. So if I deny your motions and let the jury decide them, I can always, after a verdict, reconsider; but then we have a jury verdict, so that if it is reversed, we don't have to try the case all over again. Do you know what I'm saying?

MR. HIGGINS: Oh, I understand that, your Honor. I appreciate that.

* * * *

[Page 1707, line 4 to Page 1708, line 22]

THE COURT: Let's talk about whether you really can patent an idea, though, rather than a method. If you could do this quickly. This is part of the argument. The idea that that doctor can take that high homocysteine and figure out that there is a B12 or a folate deficiency. Really what Claim 13 is.

MR. WHITEHAIR: I think there has been a misunderstanding about what this mental step might be. The mental step doctrine is pretty outdated. It turns out, in fact, that the Federal Circuit has decided that a mental step, even—as long as it in an algorithmic sequence is fully legitimate. What's really the problem with this: You remember in 1985, no one knew to make this mental step. They came out in their patent and said, Hey, look what happens if you have this high number of this special marker of the hundred thousand markers in the body. We found one that happens to be 95 percent of the time always hooked up with a B12 and folate deficiency. Wow. Now, you can go look for that marker and you can start skipping the look of all the other markers. There is this serum vitamin level, you know, B12 in your blood, folate in your blood, this homocysteine, MDS, any of that stuff. They found this one marker out of all the markers in the world. This one always responds to B12 and folate.

THE COURT: What is the invention? What is the method, not the mental step, but what is the—that's invented and why are you arguing that the Abbott test, or are you arguing that the Abbott test is covered under the patent or just under the contract?

MR. WHITEHAIR: No, unquestionably it's covered under the patent. The issue is whether Abbott is accomplishing the exact same thing that the other method was. LabCorp would like to say that they've only been paying on a royalty agree-

ment and the know-how license with Metabolite on the basis of Claims 1 through 12. That's not what the license agreement says. The license agreement very clearly divides out mass spectrometry—that's the GCMS; things covered by the claims and methods of the patent, and then there is a couple of tests that really aren't covered by the patent. And those are defined even differently as having to show some connection or correlation to B12 and folate deficiency.

* * * *

Rule 50 Motions

[Page 1727, lines 2-6]

MR. JABLONSKI: * * * I honestly think that with time and use of the jury verdict and the instructions that they can come to focus on the issues.

THE COURT: You couldn't have a brighter jury.

MR. JABLONSKI: Yes.

* * * *

Plaintiffs' Closing Argument

[Page 1769, line 24 to Page 1770, line 18]

We also see that LabCorp wrongfully terminated the Metabolite license agreement to get out of paying these royalties; and thus, the license agreement evaporates for them. That leaves us with the 21.5 percent payment for all of the assays that were done when that license agreement was wrongfully set aside and the 6 percent for all of the infringement that was done by CTI—or by LabCorp—again, when that license agreement was just shut aside.

The parties have actually gone to the trouble of coming up with a total number of Abbott assays. That's Exhibit 278. They've also totaled the actual dollar amount that has been earned on billed amounts. It comes to 16,989,000 and change. You'll see the number in the book.

CTI would ask and asks now for its 6 percent for this patent infringement or for this failure to follow the license agreement payment scheme. And 6 percent of that number comes to $1,019,364.

Metabolite: 21.5 percent on that number. And they each get their own cut at that same number because they each have an independent royalty stream. Comes to $3,652,724.

* * * *

Jury Verdict

[Page 1865, lines 8-12]

THE COURT: * * * So—and last and not least is the jury, because this is indeed one of the most complex cases that we have ever had presented in court, if not the most complex; and I think this is probably the most attentive, hard-working jury I've ever had, so I really do thank you.

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